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THE VITAMIN B REQUIREMENT OF MAN

BY

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TO

LAFAYETTE B. MENDEL

REVERED TEACHER, WISE COUNSELOR,
AND FRIEND

PREFACE

THE study of which this monograph is a report owes its origin to the interesting observation made in 1923 that the rat requires more vitamin B per unit of weight than the dog. Consideration of this fact naturally led to the question as to how much vitamin B a human being needs and the possibility of studying the problem experimentally. In a conversation concerning this matter the late Professor T. B. Osborne in his characteristic way remarked that "man cannot possibly require as much vitamin B per unit of weight as the rat; if such were the case all of us would die early from beriberi." The possibilities for human welfare resident in a study of this problem seemed to me so great that for over a decade it has been one of the themes of my research activities.

In this report I do not wish to convey the impression that I believe I have reached a perfect answer to the question. It has been necessary to employ a rather indirect approach and to make certain assumptions, many of which will doubtless be shown by future research to involve considerable error. If the results obtained in this study prove to be correct in the sense of a reasonable first approximation to the truth, I shall be satisfied. I am quite willing to be criticized for not having obtained a more highly accurate answer to what the critic will doubtless admit is a very difficult problem.

In the prosecution of this research I have had the help of many people. The early experiments with rats and dogs were conducted in collaboration with my colleague, Professor Arthur H. Smith. In certain more recent animal studies I had the coöperation of Professor Harold E. Himwich. Numerous students and research fellows assisted in many ways, particularly H. J. Deuel, Jr., H. H. Beard, B. H. Klotz, H. A. Rosenberg, J. Rogoff, A. Gilman, Ethel Burack, R. J. Block, Margaret Dann and W. Goldfarb. To Franklin Hollander I am indebted for valuable advice in the attempts to find some common mathematical relationship applicable to the data obtained from different species. When the fundamental data from animal experiments had been obtained I received much encourage-

ment from Colonel E. B. Vedder to continue the research, particularly by a study of human diets in relation to the disease beriberi. I absolve all of these persons from any responsibility for the interpretations placed upon the data. If the ideas advanced are erroneous I accept the blame. In obtaining current data relating to various American dietaries I have been given material by Professor Lydia J. Roberts and Ruth Blair of the University of Chicago, Adelaide Spohn, and Callie M. Coons; to all of these I am grateful.

Perhaps many of my colleagues in the field of vitamin research will object to the ratings which I have given certain foods based on their particular tests. In any work where an attempt is made to integrate, as it were, numerous quantitative data, obtained in different laboratories and by different methods, considerable error must be encountered. In order to enable the critic to correct such errors wherever possible, I have endeavored always to state the assumptions involved in my calculations and to indicate clearly how each particular set of data was utilized.

Not being a clinician I hesitated somewhat before undertaking to present as part of this report a statement of the clinical implications of this research. At the request of the Council on Pharmacy and Chemistry of the American Medical Association I had written a paper dealing with the clinical aspects of vitamin B. The favorable reception accorded this effort encouraged me to include in this monograph a statement of the present status of the vitamin B problem as I see it presented to the clinician. I hope that my clinical friends will accept this in the way that it is intended, namely, as suggestive of what seems worthy of clinical trial. It is important for us to know not only the possibilities but the limitations of vitamin B therapy. The status of the problem now is such that I believe the next important advances will be made by the clinician. In this connection I am pleased to record the interest which many of my clinical colleagues in the Yale University School of Medicine have shown in this work, particularly Drs. H. M. Zimmerman, E. F. Gildea, L. H. Cohen, T. G. Klumpp, James C. Fox, Jr., and S. B. Kleiner. Acknowledgement should also be made of the interest exhibited and clinical studies performed by Dr. Katherine O. Elsom in Philadelphia, and my former pupil, Dr. William B. Rose, in New York City.

Most of the animal experiments (Chapters IV, V, VI, VII and VIII) have been described in separate articles published in the *American Journal of Physiology*, and I have received permission to use this material here, either wholly or in part. Similar permission has been obtained from the *Journal of the American Medical Association* (Chapter XV) and *International Clinics* (Chapters XIV and XV) with respect to material appearing in these periodicals. Thanks are due the *Philippine Journal of Science* for permission to reproduce the photograph of a case of wet beriberi originally published by Herzog (see Fig. 1).

It gives me pleasure to acknowledge the technical assistance of H. Bronfin and Miriam M. Campbell in carrying out many of the laborious calculations involved in the evaluations of numerous human diets. Finally, I wish to thank Mr. and Mrs. M. K. Horwitt for their untiring aid in the preparation of the manuscript.

The expenses of this investigation were met by grants from various sources. In the earlier animal studies grants were made from the Russell H. Chittenden Research Fund in Physiological Chemistry and the funds of the Department of Physiological Chemistry in Yale University. The expenses of the more recent animal experiments, designed to test some of the implications of the findings then at hand, were defrayed in part by grants from the Research Fund of the Yale University School of Medicine. To the National Academy of Sciences I wish to express my appreciation for a generous grant to aid in the publication of this monograph.

GEORGE R. COWGILL

New Haven, Connecticut
June, 1934

NOTE TO SECOND PRINTING

According to Colonel E. B. Vedder, the "red rice" discussed on page 124 *et seq.* was not parboiled or cured but a fairly highly milled product made from a rice with red pericarp; and, in his opinion, the vitamin index value of 3 allowed for it is too high. Also, on page 167, the index value of 3 assigned to Philippino rice No. 2 is too low; the value ought to be from 5 to 10. If these changes are made, obviously the cases under discussion agree even better with the thesis of the book.

In order to increase the practical usefulness of this volume a table of vitamin index values of foods in terms of International Vitamin B units per gram, as well as my milligram-equivalent unit has been added as an appendix.

GEORGE R. COWGILL

New Haven, Connecticut
June, 1935

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CHAPTER I

THE PROBLEM UNDER INVESTIGATION

Man's Requirement for Dietary Factors

THE discovery that a given substance is necessary for the proper nutrition of man at once raises the question as to how much of this factor is required. If the answer to this query is known, then it becomes possible to insure at all times an adequate intake of this substance, at the same time maintaining some semblance of physiological economy when so doing. When it is known that failure of an individual to ingest a sufficient amount of vitamin B results in limitation of growth or the development of a disease, knowledge as to *how much* of the substance is needed and as to the variables that may change this value makes it possible to place vitamin B therapy on a rational scientific basis.

Dietary Standards Now Available

At the present time reasonably accurate minima of intake for human beings are known for protein, calcium, phosphorus and iron, and from such facts suitable standards with respect to these dietary essentials have been devised. Concerning the vitamins, however, practically nothing is known of an essentially quantitative nature. Numerous reasons may be cited for this. In the first place, the vitamins have been known only for a comparatively short time. New developments in the field of vitamin research have played their part in delaying the performance of quantitative studies aimed at ascertaining man's requirement. For example, the discovery that the physiological properties of what was formerly called vitamin B are due to at least two physiologically active substances, now called vitamins B (or B_1) and G (or B_2), has made it necessary that many earlier studies be repeated with a further limitation of variables. The suggestions obtained by many workers of the existence of still other hitherto unrecognized factors in the vitamin B complex have resulted in great activity in attempts to demonstrate

clearly what was previously only vaguely hinted at. Thus have the studies in this field continued to be more definitely qualitative in nature rather than quantitative.[1]

A second reason for the paucity of quantitative data relating to vitamins resides in the fact that the condition which must be studied in making the measurements usually involves the production of a disease, a fact which almost entirely precludes any organized and planned experimentation on human beings. This is in marked contrast to the situation encountered when one wishes, for example, to determine the calcium minimum in an adult human being. In such a case, experiments can be conducted, the intake of calcium varied at will, the output studied, and the amount of lime that must be ingested in order to produce an equilibrium definitely determined. The conditions of such experiments can be endured by the human subject without harm.

Data regarding man's requirements for vitamins are few because of the difficulty encountered in translating the results obtained in one species, the rat for example, to the human species, or, for that matter, to any other species. Foods may be tested for vitamin content on the rat or the pigeon, and their values relative to each other ascertained, but one cannot draw many conclusions from such tests with regard to man's need for the vitamins. In order to evaluate human diets with respect to any given vitamin, it is necessary to know not only the vitamin contents of different foods relative to each other or to a common standard, but to have some idea as to how much the human being needs. Vitamin tests of the conventional sort, conducted on one or two species of laboratory animals, supply only a part of this requisite information.

1. As a result of these developments a problem in nomenclature has arisen. American investigators, following the suggestion of the Committee on Vitamin B Nomenclature of the American Society of Biological Chemists (1929), use *vitamin B* to designate the more heat-labile, antiberiberi factor discovered by Eijkman (1897), and *vitamin G* as the name for the more heat-stable, pellagra-preventive substance discovered by Goldberger and associates (1926). British workers in this field use subscribed numbers B_1, B_2, B_3, etc., with appropriate descriptive adjectives where necessary, to indicate various members of the vitamin B complex. Under this system, the two best recognized members of the complex, namely the vitamins B and G of the American workers, are called *vitamin* B_1 and *vitamin* B_2, respectively. The study reported in this monograph deals primarily with *vitamin B*, or B_1.

Importance of Quantitative Studies in Relation to Discovery of New Dietary Factors

THERE is a subtle fallacy in much of the research which purports to prove the existence of new dietary factors, due to failure to appreciate the importance of quantitative studies in relation to the problem. It seems axiomatic that before one is justified in explaining the particular phenomena on the basis of the existence of new substances of vital importance, he must demonstrate that there has been an ample supply of known dietary essentials. In my opinion this has not always been done. The developments with respect to the hypothetical B_3 factor indicate that this critical attitude is justified. For example, in 1928, Williams and Waterman claimed the discovery of a new substance of vitamin nature in yeast, required by birds. Observations of Eddy, Gurin and Keresztesy (1930) and by Peters (1929, 1930) were interpreted as favoring this view. Inasmuch as the new factor appeared to be closely associated with vitamins B_1 and B_2, vitamin B_3 was proposed as a name for it. Its chief physiological property seemed to be that it permitted an increase in weight following the bird's recovery from the symptoms of advanced vitamin B_1 deficiency. Now, to me it appears evident that the amount of a dietary factor needed to maintain a given organism at a certain weight may be quite different from that required if the organism is to be permitted to increase in size, *i.e.*, gain weight. One can well imagine that in the latter case a larger amount of the dietary essential might be necessary, but just *how much* larger this quantity must be may be quite unknown. It may well be that relatively enormous amounts of the already known vitamin must be administered, in order to permit reparative processes to occur in tissues, and other unknown processes to take place which involve a restoration of body weight to approximately the normal value. Appreciation of the importance of this quantitative point of view, and subsequent research in relation to vitamin B_3 eventually led Williams and Eddy (1931) to state:

> Accordingly it now seems possible that the weight factor B_3 is nothing more than abundant supply of B_1, roughly ten to twenty times the minimum antineuritic requirement. On the other hand we can by no means be certain that the purest supply

of B_1 which we have available in quantity does not contain enough B_3 as an impurity to produce the characteristic result when fed in large quantities. (page 443.)

The recent studies of Morris (1933) directed toward this very question led to the following, among other conclusions:

weight recovery may be a function of quantity of vitamin B_1 rather than the effect of a different vitamin. Weight recovery was produced by increasing the dosage of B_1 sources by amounts considerably above that necessary to cure or for protection against polyneuritis. (page 22.)

The reader should not construe the above discussion to mean that I deny the existence of other dietary factors in the vitamin B complex. The point to be emphasized is that much of the evidence submitted thus far for this view is unconvincing; suitable purely quantitative data relating to the already known vitamin, if obtained, could explain the phenomena in question just as well as the absence of one or more hitherto unappreciated substances.[1]

Preliminary Quantitative Observations Bearing on the Problem

From various reports in the literature it is evident that the vitamin B requirement stands in some relation to body weight. For example, what suffices for a 100 gram rat, according to Osborne and Mendel (1922) is quite inadequate for a larger animal. Possibilities in the way of a closer approximation to an organism's requirement for vitamin B than in terms of body weight alone were suggested by a comparison of our data pertaining to the rat and the dog. In 1923, Cowgill and Deuel reported the results of experiments on the amounts of the same yeast concentrate required by white rats and dogs. Our curiosity was especially aroused by the fact that, on the basis of these experiments, rats weighing from about 80 to 160 grams were found to require approximately five times as much vitamin B per unit of body weight as the dog. Inasmuch as the basic metabolic

1. After the above paragraphs had been placed in type the paper by O'Brien (1934) appeared in which considerable evidence is presented in favor of the existence of a B_3 factor for pigeons; the existence of this new dietary essential is demonstrated under conditions where as much as 40 times the curative dose of vitamin B_1 is being given. It is interesting to observe that the factor here discussed differs from that of Eddy, Gurin and Keresztesy in being more stable toward heat. Mention of this fact serves to emphasize the complex nature of the problem under investigation.

levels of these two species stand in a somewhat similar relation to each other, there was suggested the possibility that the vitamin B requirement may be related in some way to metabolism—perhaps the number of calories metabolized—or to body-surface area, "active protoplasmic mass," or some other entity of metabolic import. Since such factors stand in certain fairly well-defined relationships to body weight, the published observations of Osborne and Mendel, and others that might be mentioned, could be regarded as confirming such an idea. The importance of an experimental investigation of this possibility will be further appreciated when it is realized that the establishment of some general relationship in several species may pave the way to a determination of man's requirement for vitamin B, and perhaps the need for other dietary essentials as well. If the rate of metabolism or some function of it is involved in the determination of an organism's requirement, and an expression valid for several species should be arrived at, then it should become possible to interpret properly for man's nutrition quantitative experiments performed on rats and other animals. This monograph is a report of such an investigation.

Plan of the Investigation

The following plan of experimentation was followed. A given vitamin B-containing preparation[1] was tested quantitatively on four species of animal, namely, the mouse, rat, pigeon and dog. The individuals in a given species varied appreciably in body weight. The minimum amount of the vitamin concentrate required by each individual was determined as carefully as possible. The several groups of data were then studied and compared with the hope that certain underlying relationships would be revealed which would suggest one or more of the factors that determine the organism's requirement for vitamin B. That such hopes were realized in surprising degree, the data submitted in the following pages clearly indicate.

A formula applicable to four widely different species having been found, it was then extended to the human species. The validity of the expression for human beings was tested in the following manner.

1. Lot 985 of Yeast Vitamine Powder (Harris) obtained from Harris Laboratories, Tuckahoe, N. Y.

Foods that have been assayed for vitamin B content were listed in the order of their value in this respect. These values were expressed in terms of the same standard, namely the vitamin concentrate used in the studies on four animal species. Various human diets were studied which were known to have been associated with (*a*) absence of beriberi, (*b*) incidence of a few cases—therefore borderline in character, and (*c*) epidemics of this disease. The vitamin contents of these diets were compared with the human requirements as predicted by the newly devised formula. As the reader may readily ascertain by study of the following pages, the agreement of the predicted requirements for vitamin B with the facts concerning the incidence of beriberi is excellent. Upon this basis, therefore, the author rests his first thesis, namely, that it is now possible to state with reasonable accuracy the minimum requirement of normal adult human beings for vitamin B.

Study of the formula, by which the human requirement for this dietary essential is calculated, indicates, as a logical implication, that *body weight*, or size, and metabolic intensity, or *metabolism*, are the most important factors determining the vitamin requirement. Animal experiments to test this corollary were performed and confirmation obtained.

Various applications of these findings in the fields of human nutrition and clinical medicine suggest themselves. These are discussed in some detail. Their complete confirmation must await the results of further coöperative effort and study, particularly by clinical investigators.

CHAPTER II

GENERAL DISCUSSION OF BERIBERI

Incidence of Beriberi

DETERMINATION of the human requirement for vitamin B is important not only because it affords a standard which the student of nutrition may apply when evaluating human dietaries, but because of its bearing on the problem presented by the disease beriberi. In certain parts of the world, notably in the Far East, beriberi is so prevalent that it constitutes one of the most serious medical problems confronting the public health authorities. The three most important regions in which this disease is endemic are Asia, South America and Africa. In his monograph devoted to beriberi, Vedder (1913) presents numerous statistics showing the distribution and prevalence of this disease throughout the world. It is not our purpose to repeat all these data here. Let it suffice to summarize them in such a way as to orient the reader to the seriousness of the problem up to that time. The presentation of new data will be confined to those that have appeared since Vedder's review.

Japan

In Japan, according to Vedder, beriberi is found in all sections, from the Kurile Islands at the extreme north to the southernmost islands of Formosa and Kyushu. In the Japanese Army in 1875 not less than 26 percent of the entire force of 17,500 men were afflicted with the disease, in other words, *approximately one soldier out of every four*. "During the Russo-Japanese War in 1905," according to Shibayama,[1] "Japan had 200,000 cases of beriberi in the army, and this was the only ravaging epidemic with which the army had to contend." According to the more recent statistics of Satow (1925) the number of cases per 1,000 soldiers in 1906 was 32.55; for 1907 the rate was 11, and for the years 1908–1921 inclusive the average

1. Vedder, p. 13 (1913).

rate was 5 cases per 1,000; in 1922 and 1923 there was a marked increase in the incidence, the rates being 11.42 and 10.47, respectively.

In the Japanese Navy during the period 1878–1883, when the total number of sailors ranged between 4,528 and 5,346, the maximum and minimum rates of incidence of beriberi in percent of the total force were 40.4 and 23.1 respectively. Following the classic experiments of Takaki there was marked improvement, the case-incidence per 1,000 sailors dropping from 231 and 127 for the years of these experiments, namely 1883 and 1884 respectively, to 5.93 for 1885 and only 0.35 for 1886 (Satow, 1925). Between 1887 and 1923 the rate fluctuated between the low value 0.11 for 1893 to a maximum of 4.77 for 1919, the average rate per annum being 1.38 per 1,000. For reasons probably related in part to the World War the rate was definitely higher during the decade 1913–1923.

I have not been able to secure recent data showing case-incidence of beriberi for the general population, although the number of deaths per annum from this cause is a matter of record. From Satow's (1925) tables it appears that the average mortality rate per 1,000 total deaths for the years 1915–1922 inclusive was 13 percent, the rate for cities with a population of 50,000 or more being roughly three to four and one-half times that for smaller communities and rural districts. Maki's (1932) data for the years 1920–1929 inclusive indicate an average death-rate for beriberi of 29.4 per 100,000 inhabitants. The International Health Year Book for 1929 lists 32 different causes of death in Japan in descending order of importance and beriberi appears as the twentieth cause in the list with a rate of 9.9 per 1,000 total deaths.[1] According to the same authority, beriberi is much more serious as a cause of death in infants; 24 causes of infant mortality are presented in descending order of value with beriberi occupying eleventh place.[2]

China

Beriberi continues to be very prevalent in southern China and comparatively rare in the northern part. According to Vedder it

1. See table 4b, page 669.
2. See table 5d, page 672.

was extremely difficult to secure accurate statistics from most sections of China. Hongkong proved to be an exception, accurate records of deaths from beriberi being available for the years 1891 to 1910. From the tables furnished it appears that in Hongkong during this period, when the city's population ranged from 198,742 to 350,975, the number of cases must have been very large.

> When we remember that the average mortality of beriberi is about 5 percent, it will be seen that the total number of cases in Hongkong must run well into the thousands. . . . We do not know that beriberi is more common in Hongkong than in other parts of China from which it has been reported, and if Hongkong, with a population of 350,000, has 10,000 cases of beriberi annually, it may be imagined that millions of cases must occur among the remainder of China's teeming population.[1]

Malay Peninsula

In the Malay Peninsula the incidence of beriberi has been very high. From the statistics collected by Braddon (1907) it appears that in the years 1895 to 1902 there were 328,936 admissions to 31 district hospitals "for all causes," and beriberi was responsible for 57,025, or 17.3 percent. The International Health Year Book for 1929 (p. 1259) reports more recent data. In 1928, with a total of 66,203 patients treated in the hospitals, 1,399 were afflicted with beriberi, or 2.25 percent; there were 236 deaths due to this disease, or 3.94 percent. These admissions for beriberi were of course those of individuals whose condition was serious enough to warrant hospitalization. These figures take no account of the mild cases that were treated at home.

Dutch East Indies

Beriberi is endemic in the Dutch East Indies. Statistics showing the prevalence of the disease in the Dutch East Indian Navy are presented in Chapter XII (see pp. 147–153) as part of a study of the dietaries in use in this naval force. In recent years, as a result of the activities of the public health service in Java, particularly with respect to increasing the use of various foods other than white rice by the civilian population, the incidence of beriberi has been greatly reduced.

1. Vedder, p. 15 (1913).

Philippine Islands

The Philippine Islands continue to be a focus of beriberi. From time to time epidemics have appeared. Prior to 1910 the native constabulary, known as the Philippine Scouts, was seriously affected with the disease; as a result of changes in the dietaries made at this time (see p. 164 *et seq.*) beriberi has practically disappeared from these troops although continuing to furnish a serious public health problem among the civilian population. For detailed statistics pertaining to Manila and the other provinces the reader is referred to the data obtained by Heiser and cited by Vedder (1913, pp. 22–23). As evidence of the present importance of the beriberi problem one may cite the International Health Year Book for 1929, in which it is stated, referring to deaths of infants in 1928, that "this disease ranks third for mortality." Beriberi has also been reported as occurring in Australia and numerous islands in the Pacific, and practically all parts of Africa.

South and Central America

In South America beriberi has appeared chiefly in the Amazon basin in Brazil as well as in the more southern countries of Paraguay and Uruguay, and along the eastern coast from the La Plata river in the south to the Orinoco in the north. It was first reported as appearing in Cuba in 1865 and in Panama in 1887.

The World War

During the World War beriberi appeared among Chinese labor battalions in France (Sicard, Roger and Rimbaud, 1917; Mauriac and Duclos, 1918), British troops in the Mediterranean Area, Mesopotamia (Willcox, 1916; Hehir, 1919; Sprawson, 1919–20), and India (Kennedy, 1915), and in the United States troops at San Juan, Porto Rico (Riddell, Smith and Igaravidez, 1919; Ashford, 1922).

The United States

Beriberi has also been observed in the United States. It was reported as appearing among New England fishermen. Public institutions have suffered from it. Bondurant observed 71 cases

in the state insane asylum at Tuscaloosa, Alabama, in 1895 and 1896. The Arkansas State Insane Hospital reported some cases in 1895. In the Texas State Lunatic Asylum during 1907 there occurred an epidemic with over 200 cases and 20 deaths. Another epidemic broke out in South Carolina in 1910; these cases occurred among the prisoners in a convict camp.

Since the publication of Vedder's monograph in 1913 there have been reports of beriberi occurring in the United States. Several cases have appeared among immigrants from the Far East, one in Chicago (Holmes and Retinger, 1916), two in California (Reed, 1917) and seven among sailors on a ship arriving in New York harbor (Abdou, 1918). Parker (1914) reported on the occurrence of 25 cases in the County Jail at Elizabeth, New Jersey. In their paper dealing with cases observed in Louisiana, Scott and Hermann (1928) attributed the disease to the extensive culture of rice in that state; their paper is also valuable because it presents statistics for the United States covering the period 1911–1919. Beriberi continues to occur in Newfoundland and Labrador, Little having reported on 220 cases in 1914, and Aykroyd (1930) on a dietary study made in relation to the disease in 1928–29. Kepler (1925) had occasion to observe beriberi in a negro woman who had voluntarily restricted herself to a diet of raw starch in the belief that this would result in the cure of a long-standing gastrointestinal disorder. Likewise Riesman and Davidson (1934) very recently reported on beriberi observed in a man 76 years old and resulting from voluntary drastic restriction of food in an attempt to relieve chronic stomach trouble. The cases just cited were definitely diagnosed as beriberi; in these instances the symptoms of this disease predominated in the clinical picture. There have been reports of cases of other disorders in which some of the symptoms were attributed to lack of vitamin B (beriberi). These are discussed in Chapter XV, p. 214 *et seq.*

This very brief presentation of the facts concerning the incidence of beriberi should suffice to indicate the seriousness of the beriberi problem, particularly in the Far East, and emphasize the significance of any investigation throwing light on the etiology, prevention, control or treatment of this disease.

Description of Beriberi

It is not our purpose to present here a detailed clinical discussion of this disease. It will suffice to call attention to the more outstanding features of beriberi in order to show the relation of this condition to that which experimenters have been able to produce in animals. The most striking symptom of beriberi is paralysis of the legs. The Chinese name for the disease is *käkke* which has been translated "disease of the legs." Likewise the term used in Malaysia, namely *kaki lem but* signifies "weak legs." From Vedder's discussion of the etymology of beriberi it is evident that this paralysis has stood out as the most impressive feature of the clinical picture. This loss of the use of the limbs may occur along with a marked atrophy of the leg muscles, in which case the condition is spoken of as dry beriberi, or it may be associated with edema and the term wet beriberi applied to it. Figures 1 and 2 are photographs illustrative of these two important types. Some authorities have described what might be called the mixed type in which the atrophy of the leg muscles is masked by the edema. Because of the leg weakness there is little disposition to walk, and in the more advanced stages of the disease the gait is a peculiar one of the "steppage" type. The legs are stiff and anesthesia of varying degree supervenes. The condition may progress until the muscles of the arms are involved and the patient becomes practically helpless. The paralysis appears to be of the spastic type. These symptoms are due to more or less extensive changes in peripheral nerves. In other words, the outstanding pathological change in this condition is a peripheral polyneuritis.

Beriberi is also characterized by certain vasomotor symptoms. A common observation relates to a very noticeable palpitation of the heart. This may be fairly constant or it may be noticed only after the strain of exercise or when the patient is reclining in bed. This cardiac palpitation is usually associated with dypsnea of varying degree. Whether the prognosis is favorable or not depends in large measure upon the prominence of the cardiac symptoms. The outstanding cardiac change observed in both the living patient and at autopsy is an enlargement of the right side of the heart.

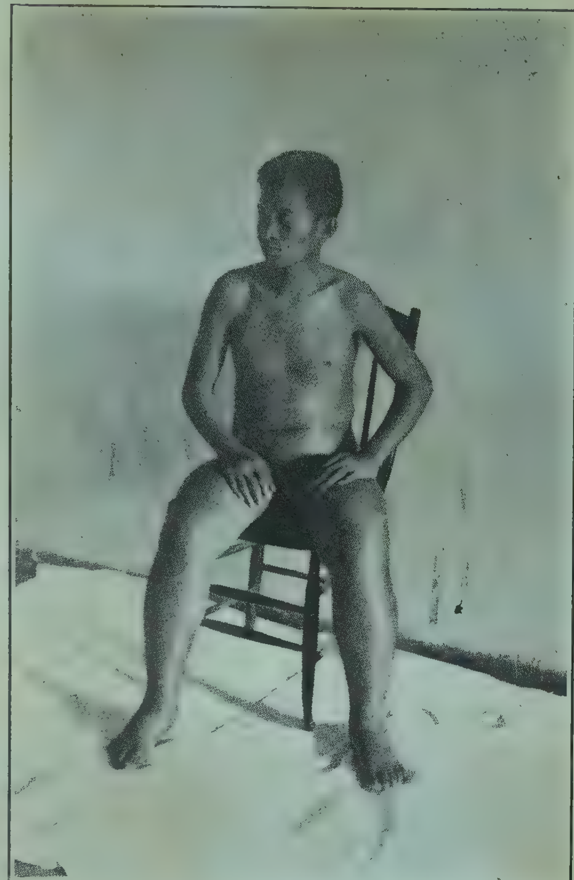

FIG. 1

Illustration of "Wet" Beriberi. (This photograph by Herzog is reproduced through the courtesy of the Philippine Journal of Science.)

FIG. 2

Illustration of the "Dry" or Atrophic Form of Beriberi. (Taken from Baelz and Miura.)

Is Beriberi Really a Deficiency Disease?

Many theories have been advanced to explain the development of beriberi. The view most widely held at the present time attributes this disease to a too-prolonged subsistence upon a diet deficient in the factor now called vitamin B. The greatest advance in this field came when Eijkman (1897) observed in fowls a condition very similar to human beriberi. The attempts of numerous students of nutrition to ascertain why a simple mixture of protein, fat, carbohydrate and mineral nutrients fails to meet the demands of growth and maintenance also played an important part. To review all of the work in this field would be a tremendous task and would serve no useful purpose here. The interested reader is referred to the monographs of Sherman and Smith (1931), McCollum and Simmonds (1929) and the many papers cited in these books for detailed presentations of this literature. As one illustration of the possibilities in the field of animal experimentation Figures 3 and 4 are presented. The reader is asked to compare these photographs (facing p. 18) of a polyneuritic dog with that of human beri-beri shown in Figure 2. An extended description of experiments such as are illustrated in Figures 3 and 4 is given in Chapter V, p. 40.

The reader may recall that the plan of the research reported in this monograph, as described in the previous chapter, involves an examination for vitamin B content of various human diets, known to have been associated with beriberi, and a comparison of the results with the human requirements for this dietary factor, as indicated by the prediction formula resulting from this investigation. Obviously this test of the applicability of our vitamin researches involves the assumption that human beriberi is fundamentally due to lack of vitamin B. This view was first proposed by Funk in 1911 and was made the thesis of Vedder's monograph in 1913. Since that time it has received more or less general acceptance. However, it must be borne in mind that even now certain groups of clinicians, notably in Japan and in South America, definitely reject this view. Because of the importance of this question in relation to the present research I now propose to examine this matter in detail in an endeavor to clarify, if possible, the issues that have been raised in relation to it. In his monograph Vedder

reviewed the early work and theories concerning the etiology of beriberi. Another valuable summary of the ideas relating to this topic will be found in the paper by Musgrave and Crowell (1922).

The Intoxication Theory

PROBABLY the oldest explanation of the origin of beriberi attributes this disease to an intoxication. Inorganic agents such as arsenic, carbon dioxide and oxalic acid have been cited in this connection. Organic substances such as the "ptomaines" and other completely unknown poisons believed to be present in common foods, especially in white rice, have been suggested. Fish is probably the food most commonly used in the Orient to supplement polished rice. Many investigators have suggested that the hypothetical poison is present in this animal food. There were reasonable grounds for advocating this view that beriberi is essentially an intoxication. Even now the clinician must be careful to exclude certain known poisons as possible causes of the polyneuritis in question. Perhaps the most valuable contribution to the beriberi literature from the standpoint of its advocacy of the intoxication idea is the extensive monograph by Braddon (1907). This investigator carefully collected all of the literature bearing on the problem of the etiology of beriberi and interpreted it as supporting the idea that this disease is due to a toxin present in white rice. Most of the evidence which Braddon collected in support of his thesis can, in my opinion, be interpreted as favoring the vitamin theory.

More recently, in an endeavor to harmonize the intoxication idea with the vitamin hypothesis, it has been suggested that the toxic agent is some metabolite produced within the organism as a result of a long-continued shortage of vitamin B. Walshe (1918) drew an analogy between beriberi and diphtheria, chiefly in relation to the heart conditions which are quite similar in these two diseases. As is well known, many of the symptoms of diphtheria are due to a specific toxin elaborated by the infectious agent. Walshe suggested that in beriberi the toxin is a metabolite which has a special affinity for cardiac tissue.

Cowgill, Rosenberg and Rogoff (1930) made some indirect attempts to test this possibility in vitamin B-deficient dogs by

experiments in which vigorous diuresis was brought about with the idea of washing out any hypothetical toxic metabolite as rapidly as it was formed. Such experiments yielded negative results so far as this theory is concerned. Teruuchi, Wada and Oyama (1929) prepared what they called "oryzatoxin" by alcoholic extraction of polished rice, and, on the basis of experiments with their extract, expressed the belief that both human and experimental beriberi are due to poisoning by this material. On the other hand, Ohmori, Okamoto, Hara, Nakamura and Kurokawa (1931) performed numerous experiments designed to test the "oryzatoxin theory." Their results confirm the view that vitamin B is an indispensable dietary factor, and suggest but do not prove absolutely, that "oryzatoxin" plays little or no rôle in the development of beriberi.

The Infection Theory

The old view that beriberi is an infection was reiterated in 1923 by Ogata and associates as well as by Nagayo, and in 1929 by Matsumura and twelve collaborators. This last-named group of investigators claimed the isolation from the stools of patients of a *Bacillus beribericus* believed to be responsible for the disease. In the single case of beriberi, which Swineford (1930) had occasion to observe in this country, the presence of this organism could not be demonstrated. A much more extensive investigation of this claim was made by de Araujo (1931) working with beriberi patients in Bahia, Brazil. This observer concluded that *B. beribericus* "cannot be stated to be the cause of beriberi in Bahia." Although these studies were negative with respect to this particular organism, it is interesting to observe that de Araujo nevertheless expressed the opinion that a vitamin B deficiency cannot be related to the disease in Brazil.

The most comprehensive review of the opinions of Brazilian clinicians as to the etiology of beriberi that I have seen is that found in the paper by Rodrigues (1919). From it one learns quite definitely that one group supported the deficiency disease theory whereas another group favored infection as the essential cause of beriberi. Evidently de Araujo's experience, reported in 1931, had led him to join the latter group. Fraga, in 1923, stated his belief

that beriberi in Brazil is an infection and not a deficiency disease. According to him the best argument to be offered in support of this view is the fact that treatment of an epidemic with neoarsphenamin gave excellent results. "How could this be true if beriberi is due to a faulty diet?" Another illustration of this point of view is seen in the paper by Couto (1926), who points out that, although rice is used in practically all parts of Brazil, beriberi is found only in the north, and that "patients recover as if by magic on change of climate, while beriberi is liable to recur on return of the patients to the focus even if they refrain from eating rice."

Other observers have taken the position that in Brazil, as elsewhere, beriberi is a deficiency disease. Frazer and Stanton long ago made the point that up to that time (1913) no one had put the dietary deficiency theory to test in Brazil as had been done in Java. Lovelace (1912) had occasion to study numerous cases of beriberi in the Amazon basin and believed the vitamin deficiency hypothesis to be unable to explain satisfactorily his observations. However, the evidence offered by Lovelace was shown by Vedder (1913–14) to be very inconclusive. Lovelace's conclusions were in fact challenged directly by Walcott (1915), who proved by suitable change of diet that his cases in the Amazon basin really represented a dietary deficiency. Walcott went further and showed by tests on chickens that the common Brazilian food "farina de agua" is markedly deficient in vitamin B.

This unwillingness on the part of many Brazilian as well as other clinicians to regard beriberi as a vitamin deficiency seems to be related to the marked association of malaria with beriberi in their experience. The same situation prevails in other parts of the world besides Brazil. For example, Cannon (1929) reported on cases in Hongkong, China, and went so far as to write that "the dry and dysenteric beriberis are really camouflaged forms of malaria, as proved by the invariable findings of the specific malarial parasites on careful examination." Any completely satisfactory explanation of the cause of beriberi must account for the frequent association of this disease with malaria and other fevers. I believe that the investigation reported in this monograph furnishes such an explanation which is in harmony with the vitamin theory. Further discussion of this point is deferred until our experimental data have been presented. (See Chapter XIV, p. 208.)

Experimental Vitamin B Deficiency and Human Beriberi: Are They the Same?

The fact that the picture of vitamin B lack in experimental animals and man is not exactly the same as that of human beriberi has been offered as an argument against the view that beriberi is a deficiency disease. Tasawa (1914) and Segawa (1914) studied this problem by comparing the condition produced in birds subsisting on a polished rice diet with that in human beriberi, and reached diametrically opposite conclusions! The former held that the two conditions were essentially different, and stressed the rôle of such factors as sex, age, climate, muscular work, and kind of rice used in the diet, in producing the human disease. The latter concluded that the two conditions were fundamentally the same disease in different species of organisms. Concerning the part played by muscular work, mentioned by Tasawa, it is pertinent to cite the experiments on dogs of Cowgill, Rosenberg and Rogoff (1931) showing that in this species muscular exercise results in a more rapid use of the tissue store of vitamin B. With respect to the rôle of the kind of rice used in the diet, one may cite the work of numerous investigators, for example that of Vedder and Feliciano (1928), as ample proof that different kinds of rice have different values with respect to their ability to allow or to prevent beriberi both in the human being and in experimental animals. In this connection I may anticipate a bit and point out that as the reader examines the calculations of diets reported in Chapters XI and XII he will encounter numerous instances where a slight difference in the vitamin value for the rice makes a great difference in the total vitamin value of the ration, and therefore its factor of safety against vitamin B deficiency.

It has been argued (Nagayo, 1923) that the demonstration of the presence of vitamin B in the tissues of dead beriberi patients constitutes strong evidence against the view that beriberi is essentially a vitamin B deficiency. I fail to see the force of this contention. Similar observations have been made in experimental animals that have succumbed to lack of vitamin B. When the results are expressed quantitatively, it appears that the amounts of vitamin B present in the various tissues of a B-deficient animal are distinctly less than those characteristic of the healthy individual, and the

different organs respond to the condition of low vitamin supply in different ways. According to Westenbrink's (1932) recent observations, the heart, liver and kidney have the highest content of vitamin B under normal conditions, the latter two evidently acting as storehouses for this dietary factor. All of the organs examined, with the exception of the brain, suffer great diminution in their vitamin content after the rats have subsisted for five weeks on a B-free diet. As confirmatory evidence one might cite the observations of Graham and Griffith (1931–32). The validity of the deficiency disease hypothesis does not require that the tissues become absolutely devoid of the vitamin before characteristic symptoms and pathology may occur, but merely that the concentration of vitamin in the various organs shall become less than a threshold or critical value.

Perhaps the best summary of the facts bearing on the question of the identity of experimental vitamin B deficiency with human beriberi is that made recently by Shimazono (1931), whose observations extended over a period of years. As features common to these two conditions he lists the following: (*a*) paralysis and pathological changes of the peripheral nerves and muscles; (*b*) lowering of the minimal blood pressure, audibility of the crural tone and appearance of an epigastric pulsation; (*c*) slight hyperglycemia; (*d*) decrease in concentration of blood catalase; (*e*) decreased respiration of surviving erythrocytes; (*f*) decrease in the difference between arterial and venous blood with respect to oxygen content; (*g*) increase in blood lactic acid; (*h*) appearance of edema in both beriberi and experimental B-deficiency in man, with a slighter tendency for edema to develop in experimental animals; (*i*) varying secretion of gastric juice; and (*j*) the *striking healing action of vitamin B* preparations which occurs in both conditions. Findings which are not common to the experimentally induced vitamin B deficiency and the human disease beriberi are summarized by Shimazono substantially as follows: (*a*) Heart *changes* are much more striking and characteristic of human beriberi. (*b*) *Gastro-intestinal symptoms* are not always the same. In vitamin B deficiency, produced experimentally in both animals and man, loss of appetite, nausea and vomiting occur. In human beriberi such severe dyspeptic phenomena do not occur ordinarily except in the acute

FIG. 3

Polyneuritis in the Dog Resulting from Subsistence on a Diet Adequate Except for Vitamin B (B_1). A very slight paralysis involving the hind limbs became evident on the 60th day; on the 74th day the paralysis became pronounced. The photograph was taken on the 83rd day. At no time did this animal exhibit clonic spasms such as occurred in the dogs shown in Figures 5 and 6 (p. 46) and 7 and 8 (p. 228). This difference in the picture exhibited by dogs is similar to the differences shown in cases of human beriberi. This picture should be compared with that in Figure 2 (p. 12). (Photograph reproduced here through the courtesy of the *American Journal of Physiology.*)

FIG. 4

Another Photograph of the Animal Shown in Fig. 3, the Picture Being Taken with the Dog in a Reclining Position. Notice that the contracture of the muscles of the hind limbs is maintained even when the animal is lying down. (Photograph reproduced through the courtesy of the *American Journal of Physiology.*)

form called *Shoshin* in the Japanese clinical literature. In animals suffering from B deficiency either diarrhea or constipation may occur; in human beriberi constipation is more common. (*c*) *The blood cell changes are inconstant.* Anemia does not occur in man and the rat subsisting on diets lacking vitamin B; in the bird and the rabbit it is observed. In human beriberi lymphocytes decrease, often the eosinophil cells as well but in lesser degree, and the platelets quite definitely, whereas in B deficiency in the rat the lymphocytes, polymorphonuclear leucocytes and platelets are all distinctly decreased. In experimentally induced B-deficiency in man no definite changes in these blood cells occur. (*d*) The *basal metabolism* is reduced in B-avitaminosis in animals and man, whereas in human beriberi it varies with other conditions. The majority of beriberi cases with slight motor and sensory loss, as well as those with more or less manifest edema, show a value of the basal metabolism that is within normal limits; in cases with marked paralysis the basal rate is distinctly lower. On the other hand, when there are marked cardiovascular symptoms, the rate is increased. This pathological rise and fall of the basal metabolic level in beriberi is rapidly abolished and a return to the normal value brought about by administration of vitamin B. (*e*) The decrease in *body weight*, so constant a finding in experimental B-deficiency, is not a striking characteristic of beriberi, and is found chiefly in the "dry" form of this disease. This is an important fact and one of the reasons why many pathological anatomists have not identified human beriberi with simple vitamin B deficiency. The atrophy of internal organs occurs, however, in inanition, and in the experimentally produced condition is related to the loss in body weight. (*f*) The *changes in the adrenal* glands are not the same. Hyperplasia of the adrenal medulla is a constant finding in B-deficiency in all animals, but in human beriberi it is not striking. Here one often observes a distinct hypertrophy of the adrenal cortex. "From this comparison between B-deficiency and beriberi" says Shimazono, "it is evident that these two conditions are closely related. . . . If the cases of experimentally induced B-avitaminosis in men were to come to our clinic and their histories were unknown, we would diagnose them as beriberi."

One reason why the clinical picture of human beriberi is not

always the same and does not always agree with that of experimental B-deficiency resides in the fact that the clinical condition is very likely to be a complicated one. Many of the studies conducted in the laboratory are not quite comparable to those made on cases of beriberi. The investigator working with animals endeavors to limit the variables operating in his experiment. In the case of clinical studies, however, such uniform conditions are not likely to be obtained. A dietary deficiency in a human being is much more likely to be a complicated condition. It is not to be presumed that many individuals live on precisely the same diet as, for example, a group of rats used in a nutritional investigation. It is not surprising, therefore, that the clinical condition should show such marked variations and that it should fail often to agree with the picture of B-deficiency induced in experimental animals. All of this could be quite true even if clinical beriberi and the experimentally-produced condition were identical in the one respect, namely that lack of vitamin B was the chief etiologic factor.

It has been claimed that the failure of some cases of human beriberi to respond to vitamin B therapy is proof that lack of this dietary factor is not the essential cause of the disease. In reply to this it is pertinent to point out, first, that a complicated rather than a single deficiency may be in part responsible for this result, and second, that even in experimental animals this may occur due to failure of the administered vitamin to reach the most vitally situated lesions soon enough. Whereas the administration of vitamin B by mouth may be quite ineffective or result in only a gradual improvement, parenteral injection of the therapeutic agent usually brings about remarkable cures. Occasionally, for reasons not clearly understood, some pigeons and dogs fail completely to respond to vitamin therapy. It is possible that irreparable damage to vital functions has occurred, in which case no cure is possible. It is pertinent to point out that most of the vitamin preparations that have been used for treating human beriberi have not been suited for parenteral administration, and therefore a larger percentage of failures of vitamin therapy might reasonably be expected. Shimazono (1931) expressed the opinion that in the early trials of vitamin B therapy in human beriberi too small doses were used. The recent perfection of methods for preparing vitamin

B concentrates suitable for injection should lead to more extensive trials of this type of therapy and contribute much toward the solution of this controversy. The very fact that up to now so many cases of human beriberi have responded readily to treatment by vitamin concentrates constitutes a powerful argument for the view that beriberi is fundamentally a deficiency disease, and that lack of vitamin B is the most important factor in its etiology.

CHAPTER III

ANIMAL EXPERIMENTS: GENERAL METHODS

Critique of Methods Available for Assay of Vitamin B

FOUR main procedures have been commonly employed to determine the presence of the antineuritic vitamin in natural foods, and chemical fractions that have undergone various treatments. The *protective test* involves an estimation of the amount of the substance under assay required to prevent the development of symptoms of polyneuritis, when supplementing a vitamin-free diet. In the *weight-maintenance test* one measures the amount of material under examination required as a supplement to a vitamin-free ration in order to maintain the animal at a fairly constant body weight. One may also adopt the *curative* test which consists in determining the amount of the test material required to bring about complete relief of the neuromuscular manifestations of polyneuritis due to lack of vitamin B. It is possible to study the *growth* of young animals subsisting on diets deficient in vitamin B and to determine the amount of the substance under assay needed either to permit maintenance of body weight for an appreciable period or growth according to a selected standard, or to promote recovery after growth has ceased and a decline in body weight has set in. If one considers, in addition to these numerous procedures, the different species of animals on which the biological tests may be made, the number of possible techniques increases considerably.

None of the methods hitherto employed can be regarded as entirely satisfactory. Different groups of workers therefore, have favored different procedures for various reasons. In the early work on vitamin B the protective test was employed. Thus Eijkman (1897) used this method when he studied the beriberi-like condition appearing in his barnyard fowls. Likewise, Vedder and Clark (1912), Cooper (1912, 1914) and Chick and Hume (1917a, b; 1919) made their tests by this method. In their work which led

to the isolation of vitamin B, Jansen and Donath (1926) used the protective as well as the curative technique on both pigeons and bondols (rice birds). The chief difficulties encountered here concern the length of time required for a satisfactory test and the large amount of test substance that is needed. The interpretation of negative results is also difficult. If a given bird fails to develop symptoms in the time required by most individuals, one cannot be sure that this bird would have become polyneuritic even upon such a diet as polished rice alone. Furthermore, the long time required for the test makes it possible for other deficiencies besides that of antineuritic vitamin B to develop unless the experimental ration is very carefully constructed; certainly, where the diet is only polished rice, this objection becomes very serious indeed.

With respect to the curative test, the chief objections have been: (*a*) that administration of certain non-vitamin chemical substances may result in a complete but temporary recovery from symptoms (Funk, 1913; R. R. Williams, 1916); (*b*) that spontaneous cures (Kon, 1927) occur occasionally; and (*c*) by administering large amounts of water, thus "washing out" vitamin from the tissues, symptoms of vitamin B deficiency may be produced even in starving birds (Chamberlain and Vedder, 1911; Chamberlain, Bloombergh and Kilbourne, 1911; Eijkman and van Hoogenhuijze, 1916; Marrian, Baker, Drummond and Woollard, 1927). Peters (1924) and Roche (1925) have been able to obtain temporary recovery from polyneuritic symptoms by raising the body temperature of the animal, as well as by administering glucose; the former investigator takes account of these conditions and controls against them when performing the curative test under what he considers to be the correct conditions (Kinnersley, Peters and Reader, 1928).

Objections may also be offered against the weight-maintenance test. Perhaps the most important criticism is that advanced by Peters (1924), who pointed out that this criterion involves the assumption that the dietary factors needed for the cure of polyneuritic symptoms and for maintenance of body weight are the same, an assumption that requires proof. It is evident that the adequacy of the basal ration in other respects than vitamin B is of great importance here. Using the diet described by Block, Cowgill and Klotz (1932), the writer recently assayed a sample of the

new international standard vitamin B adsorbate by both the weight-maintenance and the curative techniques and obtained practically identical results. This indicates that under suitable conditions the weight-maintenance test can yield satisfactory results. The data obtained in these tests are summarized in Table 1.

TABLE 1

Assay of International Standard Vitamin B Adsorbate by the Weight-Maintenance Technique and by the Curative Test

METHOD OF ASSAY	PIGEON NUMBER	BODY WEIGHT			PERIOD OF TEST	DOSE, DAILY	PIGEON UNIT, AMOUNT DAILY FOR A 300 GRAM BIRD*
		Initial	Final	Average			
		grams	*grams*	*grams*	*days*	*mgm.*	*mgm.*
Weight maintenance	300	224	219	224	13	20	32.5
	326	239	240	247	13	20	27.7
	328	275	269	269	12	20	24.0
	302	268	268	275	14	20	23.1
	328	311	312	312	7	25	23.4
	320	311	310	317	11	15	13.1
	319	329	335	333	10	30	27.1
	322	375	370	373	10	20	13.9
							av. 23.1 (±4.8)
Curative test	259	...	...	180	5†	(60)	28.1
	326	...	...	205	6	20	37.7
	325	...	...	240	4	25	36.3
	326	...	...	243	5	1 of 30; 4 of 20	28
	304	...	...	270	5	(90)	21
	319	...	...	290	5	25	26.5
							av. 28.2 (±4.5)

* Calculated from formula VIT = K . $W^{\frac{2}{3}}$.

† Days over which cure was maintained when a single dose—number in parentheses—was given; in other cases, the number of days over which the bird was kept free from symptoms by daily administrations of the adsorbate.

Criterion of Vitamin B Deficiency Used in These Studies: Anorexia

In selecting a suitable criterion by which to judge whether a state of antineuritic vitamin B deficiency exists in our test animals, it was decided to consider the appearance of the subtle anorexia that develops in the absence of this vitamin, as the sign that the organism's requirement for this accessory factor is not being met. This criterion has several advantages. In the first place, it is

usually the earliest sign to appear. Therefore, exhibition of it by experimental animals means in most cases that the state of vitamin deficiency existing in the given organism is relatively mild; the animal is not, therefore, in an extremely abnormal condition as is the case when the lack of vitamin is so great as to result in neuromuscular manifestations and degenerative changes. In our experience failure of this symptom to appear is of quite rare occurrence. Furthermore, in our earlier vitamin experiments of a quantitative nature, where this anorexia was selected as the physiological sign to be watched for, quite uniform results were obtained; this was in contrast to the wide variations shown by the data secured when cure of the serious neuromuscular manifestations was the criterion employed. We soon became impressed with the fact that it is much more difficult to compare satisfactorily different polyneuritic pigeons and dogs with respect to the severity of their states of vitamin B deficiency.

Another reason for selecting this anorexia as the criterion of vitamin B deficiency for this investigation lay in the fact that the plan of study called for quantitative observations to be made on several animal species. Not all of the common species of laboratory animals develop the classical picture of extreme vitamin B deficiency with the same ease. Polyneuritic symptoms are produced with little or no difficulty in the pigeon and the dog, but not so readily in the rat and the mouse. In the two latter species, particularly in young individuals, general inanition seems to be the most common result of subsistence on a vitamin B-deficient diet; too often the animals rapidly lose weight and die without exhibiting the characteristic picture of polyneuritis. The difficulty which different investigators (Woollard, 1927, 1932; Prickett, 1934) have had in producing the pathological degenerative changes characteristic of lack of vitamin B in the rat may also be cited in this connection. The fact that inanition is so readily produced supports the view that in the young rat and mouse anorexia due to lack of vitamin B occurs with sufficient certainty to allow its use as the criterion of the existence of a state of vitamin B deficiency.

In applying the anorexia criterion to the pigeon the feeding technique was so planned as to insure as far as possible an adequate intake of all known dietary essentials except energy, which was

supplied by polished rice, and antineuritic vitamin B, which was furnished by the yeast vitamin concentrate in carefully measured amounts. The birds were weighed daily except Sundays and holidays. When a steady daily loss in body weight occurred, it was reasoned that anorexia had developed and the bird was not eating the amount of rice necessary to meet its energy requirement. The dose of vitamin concentrate given daily was then increased by a carefully measured amount and the potency of the preparation in checking the decline in weight was studied.

The pigeon data reported here were obtained in 1926. Williams and Waterman (1928) and Eddy, Gurin and Keresztesy (1930) have since claimed that birds require a hitherto unrecognized third water-soluble factor. Reëxamination of our diet and general feeding plan in the light of these reports indicates that, if such a factor (or factors) exist, our diet contains it. The details of our pigeon feeding technique are described elsewhere (see page 31).

In the dog, under certain conditions (see page 42) the anorexia due to lack of antineuritic vitamin B is readily produced and lends itself to quantitative measurements of the type desired for this investigation.

In the case of rats and mice, failure of the growing animal to make its normal gain in body weight over two weighing periods, *i.e.*, a period of one week, was regarded as indicating that anorexia had set in, resulting in insufficient food intake. The dose of vitamin concentrate being administered daily was then increased by a measured amount. It is of interest to point out here that the vitamin measurements made in rats and mice pertain to growing animals whereas those made on the pigeons and dogs were made on adult individuals. This point is of significance when endeavoring to interpret the entire mass of data and will be discussed later.

In performing quantitative experiments of the type described in this monograph it is very important that one estimate the *minimum* amount of vitamin-containing material required by the test animals. Cases where an appreciable excess over and above the minimum has been given are of little or no value for attaining the objective of this research.

Is This Anorexia Due Solely to Lack of Antineuritic Vitamin B?

These experiments were completed in 1926 when our supply of lot 985 of Yeast Vitamine Powder (Harris) became exhausted. At that time it became evident from the work of Smith and Hendrick (1926), Goldberger, Wheeler, Lillie and Rogers (1926) and others (see S. Smith, 1928) that the different biological properties hitherto attributed to vitamin B are really due to more than one substance. What was formerly designated vitamin B may well be called the vitamin B complex, in which occur at least two substances, the antineuritic factor (*vitamin B* of the American workers and B_1 of the English investigators) and the heat-stable "pellagra-preventive" "anti-dermatitis" factor (*vitamin G* or B_2). Williams and Waterman (1928) and Eddy, Gurin and Keresztesy (1930) have claimed the existence of a third factor in the vitamin B complex, a B_3, a substance required along with vitamin B_1 to secure weight maintenance in birds. More recent work (Williams and Eddy, 1931; Morris, 1933) has failed to confirm this.[1] Carter, Kinnersley and Peters (1930a, b) made a study of the supplements required to secure weight maintenance in pigeons fed on polished rice and concluded that still another factor is required, distinct from that described by Williams and Waterman (1928), and Eddy, Gurin and Keresztesy (1930). According to Reader (1929, 1930) factor B_4 is required by the rat. The fact, however, that the crystalline preparation of antineuritic vitamin B_1 prepared by Jansen and Donath (Jansen et al., 1930) from rice polishings proved effective as B_4 in a daily dose as small as 0.002 mg., supports the view that the phenomena cited as proof of the existence of B_4 are really due to lack of antineuritic B_1.

Carter, Kinnersley and Peters (1930b) made a study of the supplements required to secure weight maintenance in pigeons fed on polished rice and concluded that still another factor is required; they called it vitamin B_5. Jansen and Donath (1927) fed to their birds polished rice supplemented with meat powder and cod liver oil, and found that under these dietary conditions their crystalline vitamin B_1 protected against loss of weight as well as the develop-

1. See also footnote on page 4.

ment of neuritic symptoms. Inasmuch as our feeding technique with the pigeons was essentially the same as that employed by Jansen and Donath, lack of the hypothetical B_5 factor was not operating in our studies.

There remains for discussion the possibility that shortage of vitamin B_2, the "antidermatitis" factor, played some rôle in our anorexia studies. In the case of the pigeons, this could hardly be true because the meat powder contained this vitamin. With respect to the studies made with rats and mice the evidence bearing on this question is indirect. The basal diet used in these studies did not supply vitamin B_2. The vitamin concentrate used in these tests supplied both B_1 and B_2. Graham and Griffith (1931–1932) have observed that rats subsisting on diets rich in B_1 but low or devoid of B_2 require relatively long periods in order to deplete the body tissues of the B_2 factor; when the diet contains B_2 but lacks antineuritic vitamin B_1, there is tissue depletion of B_1 in about 30 days. The observations of Cowgill, Rosenberg and Rogoff (1931) and Burack and Cowgill (1931) pointing to lack of antineuritic vitamin B_1 as the cause of the anorexia under discussion have been extended and confirmed by studies of the effect of parenteral administration of vitamin B_1 concentrate to dogs subsisting upon a diet adequate with respect to vitamin B (B_1) but devoid of, or extremely low in content of G (B_2). As a result we may say, that lack of antineuritic vitamin B_1 is the sole reason for development of this characteristic loss of the urge to eat which was used as the criterion of B-deficiency in these studies; the "antidermatitis" factor, B_2 (G), appears to play no part, a conclusion further substantiated by the findings of Sherman and Sandels (1931). The data obtained in these quantitative studies may therefore be regarded as applying to the antineuritic component of the vitamin B complex.

CHAPTER IV

ANIMAL EXPERIMENTS: VITAMIN B (B_1) TESTS WITH THE PIGEON

Critique of Methods

Voluntary versus Forced Feeding

THE first problem which presented itself concerned the method of feeding the pigeons. In many of the earlier investigations forcible feeding was resorted to, because this may be carried out with ease in birds and results in fairly uniform production of the classical picture of extreme vitamin B (B_1) deficiency. In the pioneer work polished rice was practically the sole food because the investigator's objective was to simulate as much as possible the diet used by most beriberi patients. More recently, Simonnet (1921) and Sugiura and Benedict (1923) using purely "synthetic" diets, forcibly fed their birds, but these workers were not engaged primarily in quantitative vitamin B studies. Forced feeding is often necessitated by the very nature of the diet. If, on a ration otherwise complete, vitamin B_1 is not forcibly supplied apart from the rest of the food, anorexia very soon develops and the crop must be stuffed, if the experiment is to be carried on for any prolonged period of time. It is obvious that this practice is undesirable if one wishes the food intake to be governed entirely by the animal's urge to eat. Furthermore, Kon and Drummond (1927) made a special study of the forced feeding technique and came to the conclusion that eventually a paralysis of the crop develops constituting a factor that must be considered when endeavoring to interpret the results.

Spontaneous feeding, on the other hand, is a relatively simple and quite satisfactory method with such animals as the rat and the dog. The work of Karr (1920) and Cowgill (1921) fully illustrates this point. Experiments of long duration in which the pigeon has voluntarily eaten a completely artificial diet have been successfully carried out by Hoet (1922, 1923) and by Simonnet (1921).

The former author, in reference to following the course of the birds, attached very much importance to the weight curve. He said:

Of all the symptoms, the first, also the most constant and most regular, to which we attach the most significance, is the fall in the weight curve. One sees it decline in a slow and progressive manner; also, as soon as the yeast is restored, it rises rapidly to reach its normal level. These variations . . . are valuable only in fact if one maintains rigorously identical the state and the nature of the food before and during the experiment, so as to remove all psychic influences, and if the pigeon feeds itself spontaneously without necessitating recourse to gavage. (*1922.*)

Elsewhere (1923) in this same connection Hoet states that

in rats the loss of appetite is slow and is shown on the weight curve after several weeks; the loss of appetite in the pigeon is immediate. One can measure appetite either by food intake or by the variations in the weight curve. In the second case, the figures obtained present some comparable variations. (*1923, p. 221.*)

This author also emphasized the superior value of experiments which deal with the maintenance of the nutritive equilibrium over those which are preventive or curative of nervous symptoms. Emmett and Peacock (1925) reported that

the pigeon, judged by the weight curve, as well as the prevention of polyneuritis, can be used to determine quantitatively the vitamin B with as fair a degree of accuracy as the rat. Whether the basal diet of the pigeon is polished rice, or one high or low in carbohydrates, or the same as the regular vitamin B deficient ration generally given rats, does not seem to alter the conditions to any essential degree.

This is somewhat contrary to the views of Braddon and Cooper (1914a, b) and others who believe that more vitamin B is required on a high carbohydrate diet. In fact this topic has been the subject of considerable controversy, further discussion of which is given elsewhere (see page 73). Apropos of this contention it may be remarked here that the degree of accuracy of the measurement of the vitamin B_1 requirement, in my opinion, is not great enough to enable one to demonstrate conclusively the thesis of Braddon and Cooper, and Funk (1914). As we shall show in a later chapter, however, the observations of Braddon and Cooper, Funk and others who have related vitamin B (B_1) function to carbohydrate metabolism, are readily explained if one relates the amount of vitamin required to the total caloric value of the ration and the

body weight of the animal, rather than the carbohydrate content of the diet. Curiously enough, this was the point of view first expressed in the initial paper by Braddon and Cooper; later, in the same communication, carbohydrates were suggested as the foodstuff primarily involved, and this latter suggestion, rather than the former, seems to have been more definitely favored in the literature appearing subsequently.

In regard to the food intake, it appears that neither Hoet nor Simonnet made exact daily measurements for each pigeon. The former stated that approximately 60 to 70 grams of food on the average were consumed daily; the latter reported that 60 to 100 grams of food were eaten per day. From the lack of protocols in this respect, together with the manner in which the birds were caged—3 to 4 in a single cage—it is likely that the daily food consumption was not measured very accurately. More recently Pilcher and Sollmann (1925) measured the amount of rice consumed daily by each pigeon.

In the experiments about to be described no attempt was made, desirable as it would have been, to measure the food voluntarily eaten by the pigeons. To do this accurately did not seem feasible with the ration that was used, or even with a synthetic diet that might have been made into an appetizing paste, in view of the pigeon's habit of scattering its food. As a result it was possible neither to determine the caloric requirement nor to follow the appetite by the food intake method. It was then decided to follow the appetite by observing at frequent intervals the body weight which quickly and distinctly declines with failure to eat.

The Diet Used

In much of the vitamin B work with pigeons, polished rice has constituted the sole ration used. Use of this procedure by the earliest workers in this field was justified by the desire to simulate as far as possible the food used by those large groups of the population in which human beriberi so often appeared. With the subsequent development of knowledge by students of nutrition concerning the dietary factors that must be supplied in order to secure satisfactory nutrition, the use of such a basal diet for the pigeon by workers in this field merits serious criticism. It has been known for

a considerable period that polished rice is not a complete food; that it is deficient not only with respect to antineuritic vitamin B, but is low in protein, mineral nutrients, and fat-soluble vitamins as well. In view of these facts, it appears logical for the investigator in this field who wishes to use polished rice in his diet, because birds will pick it up readily, to supplement it as well as possible so as to supply a food mixture deficient only with respect to the one variable of interest, namely, antineuritic vitamin B. This we attempted to do. Our approach to the problem therefore differed from that of Seidell (1917, 1922), Funk and Paton (1922), Kinnersley and Peters (1925), Williams and Waterman (1928) and others, because these investigators experimented with polished rice supplemented simply by various vitamin B extracts in an endeavor to secure maintenance nutrition in the pigeon. Even Carter, Kinnersley, and Peters (1930a, b) in a recent study fed polished rice supplemented only with such products as cod liver oil and various extracts containing antineuritic vitamin. They concluded that antineuritic vitamin B alone as the supplement for polished rice does not afford maintenance. This may very well be the case. It is important in this connection to note, however, that Jansen and Donath (1926) found that their crystalline vitamin preparation made from rice polishings did not affect weight maintenance in birds fed polished rice unless this food was fed along with another substance (or substances?) which could be furnished in their experience by meat powder thoroughly extracted with boiling water. From this it appears obvious that the weight maintenance technique with the pigeon may be of service in the assay for antineuritic vitamin, provided the birds also receive meat residue, cod liver oil, and a suitable salt mixture as part of their basal ration.

The inadequacies of a sole diet of polished rice are also revealed by the behavior of birds restricted to this ration for more than about a month. Carter, Kinnersley, and Peters (1930a, b) comment on this fact. When, therefore, investigators feed birds for approximately two months on polished rice supplemented only by the products under assay, as has been done by Williams and Waterman (1928), it is not surprising that the birds, although relieved of their polyneuritic symptoms, fail to regain lost weight, an observation which has been interpreted as suggesting the existence of new hitherto unappreciated dietary essentials.

The diet which we used is as follows. Polished rice was offered *ad libitum* simply as the chief source of calories which the birds would readily pick up voluntarily, when anorexia was not present. Inasmuch as polished rice is deficient or low in protein and salts, as well as vitamins in general, a daily forced administration of an artificial food mixture designed to satisfy the protein and other minima was made. The supplementing mixture contained commercial meat residue as a source of protein practically free from vitamin B (Osborne and Mendel, 1917; Cowgill, 1927), and the Osborne and Mendel (1917) salt mixture. Practically all investigators agree that vitamin C is not necessary in avian nutrition (Simonnet, 1921; Hoet, 1922; Emmett and Peacock, 1923; Sugiura and Benedict, 1923). Concerning vitamin A, such good agreement is not the case. Emmett and Peacock (1923) and Sugiura and Benedict (1923) agreed that the pigeon needs little, if any, of this vitamin; but the former disagree when the latter state that vitamin A is dispensable in all avian nutrition, and are supported in their contention by many investigators (Plimmer, Rosedale and Raymond, 1923; Hart, Steenbock and their collaborators, 1924; Dunn, 1924). In view of this lack of unanimity and in order that fat-soluble vitamins should not be limiting factors in these experiments, cod liver oil was included in the dietary. Two to four drops were given daily either in the gelatin capsule containing the meat residue and salt mixture or that holding the test vitamin powder or administered to the bird separately with a medicine dropper. Vitamin B, the limiting factor, was supplied daily in known quantities in the form of Yeast Vitamine Powder (Harris). The error in the weighing of the doses was not greater than 0.5 mgm. Tap water and roughage, furnished by stone grit, were supplied *ad libitum.*

Inasmuch as the administration of these supplements was designed to meet the deficiencies of the polished rice, it is pertinent to consider whether the quantities of the respective supplements contained in each capsule were sufficient. About 7 percent of polished rice is protein (Rosenheim and Kajiura, 1908). From the weights of numerous filled capsules and the nitrogen content of the meat residue it is estimated that each capsule furnished about 0.9 gram of meat residue protein. It is assumed that the birds will adjust their energy intake according to their energy demands, inasmuch as this occurs in other species such as the dog (Cowgill,

1928) and the rat (Osborne and Mendel, 1918b; Smith and Carey, 1923) and seems to be a fundamental reaction of organisms. Therefore pigeons ranging from 250 to 600 grams of body weight will consume from 52 to 93 calories per day, or from about 14 to 25 grams of rice, and receive from 1 to 1.8 grams of rice protein per day. The total amount of protein ingested daily will thus range from 1.9 to 2.7 grams. On this basis the protein calories constitute from 15 to 12 percent of the total, the higher figure corresponding to the smaller birds which are the ones commonly used. Students of nutrition are aware that this level of protein intake is quite sufficient. From this it is evident that our feeding technique guarded against any loss of body weight due to shortage of protein.

The requirement for inorganic nutrients was met by means of the Osborne-Mendel (1917) salt mixture. This material filled the concavity of the end of the capsule and weighed on an average from 0.075 to 0.1 gram. Fat soluble vitamins A and D were supplied, as already stated, by from 2 to 4 drops of cod liver oil, amounts which were unquestionably adequate.

The question arises as to whether this scheme of feeding prevents any possible weight loss by the pigeon due to lack of the heat-stable "antidermatitis" vitamin B_2 or G. Inasmuch as both muscle (Hoagland and Snider, 1930; Goldberger, Wheeler, Lillie, and Rogers, 1926) and a meat-residue preparation even more highly extracted than the product used in these experiments (Vars, 1931) have been found to contain fair amounts of this heat-stable substance, it must be concluded that this method of feeding supplied some vitamin B_2 (G). At the present time there does not appear to be any satisfactory method by which one may calculate the vitamin B_2 (G) requirement in order to determine whether the amount of meat residue given our birds daily supplied adequate amounts of this factor. Consideration of the findings of Graham and Griffith (1931–1932) that relatively long periods are required to secure tissue depletion of vitamin B_2 (G), taken in conjunction with the fact that our birds received appreciable amounts of this factor daily makes it very unlikely that a shortage of this dietary essential played any rôle in bringing about loss of body weight in our pigeons. The fact already cited (see page 28), that later experiments of Cowgill, Rosenberg and Rogoff (1931), Burack and Cowgill

(1931), and Sherman and Sandels (1931), indicate vitamin B_2 to play no part in the production of the anorexia characteristic of so-called vitamin B deficiency, further supports the view that our birds did not suffer from lack of the heat-stable B_2 factor.

We have already discussed the question as to whether lack of the hypothetical vitamins B_3, B_4 and B_5, may have operated to produce loss of weight in our pigeons (see page 27).

Experimental Data

Twenty-three pigeons of mixed breeds and weighing from about 300 to 635 grams were used in these experiments. For the first two weeks all of the birds received only polished rice, stone grit and water *ad libitum*. This was done in order to deplete the tissue store of vitamin B (Osborne and Mendel, 1923). Our experience has indicated that about ten days subsistence on a diet lacking the antineuritic vitamin is necessary in order to exhaust the pigeon's supply of this dietary essential. Pilcher and Sollmann (1925) have reported a similar finding. After this preliminary vitamin-depletion period the artificial mixture of meat residue, salt mixture and cod liver oil was administered in a gelatin capsule (No. 000), one capsule being given each bird daily. The birds were weighed daily except Sundays and holidays. When the administration of the supplementing artificial mixture was begun, the birds were classified in three groups according to body weights and the vitamin powder given daily to these groups in 30, 60 and 90 mgm. doses respectively.

As illustrated on the curves presented in Chart 1, the doses of vitamin used at first were too small and the birds declined markedly in weight. It became necessary to give a few enormous doses of vitamin—see Chart 1, "large doses of yeast"—in order to save the pigeons and to allow them to regain the weight that had been lost. Larger doses of vitamin than those originally selected were then given and changed from time to time until the amount required to maintain the body weight at a practically constant level for a week or more was found. For example, the dose for bird 27, Chart 1, was finally determined to be 90 mgm. per day for a body weight of 420 grams; the correct daily dosage for bird 38 was considered to be 100 mgm. for a body weight of 465 grams. In the same way the data

summarized in the last two columns of Table 2 were obtained. It will be noticed that following the administration of enormous doses of vitamin long periods approximating three weeks elapsed before

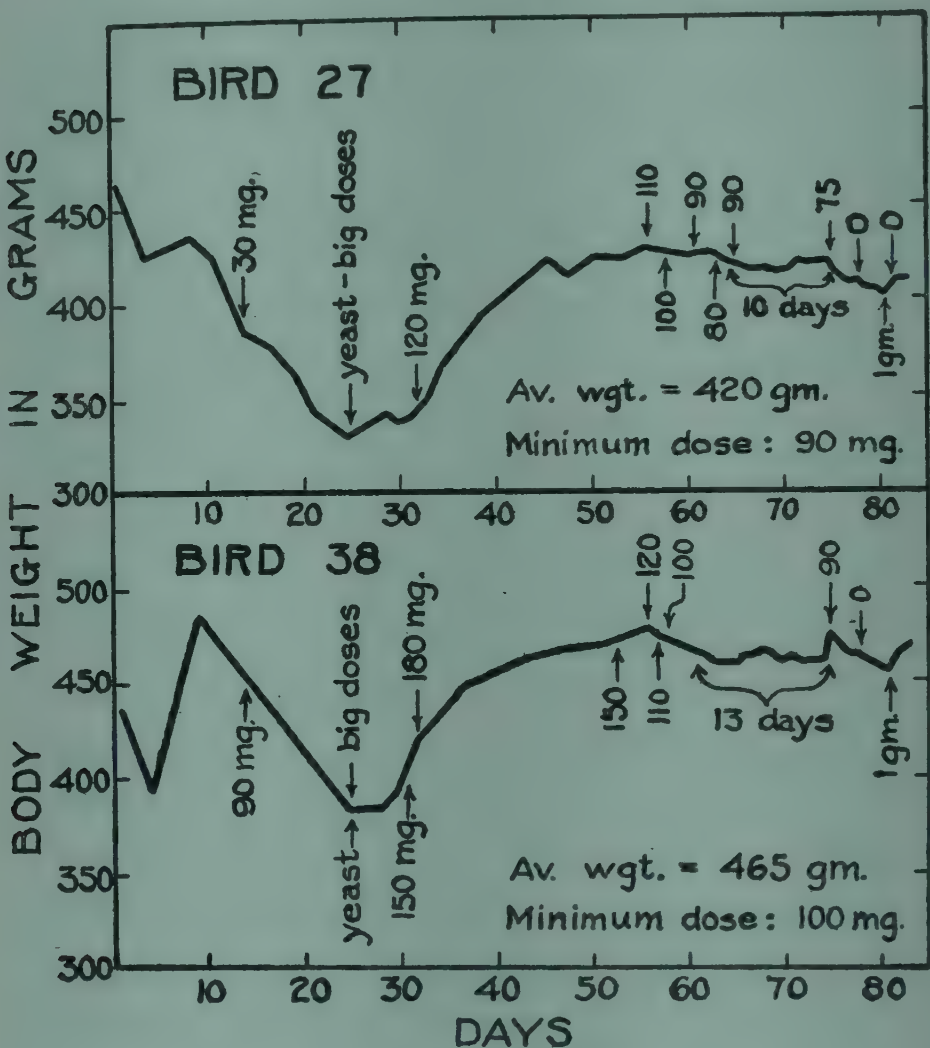

CHART 1

Illustrations of the Pigeon Weight-Maintenance Technique for Assay of Vitamin B (B_1). These graphs are based on the data obtained from pigeons No. 27 and 38.

making the slight changes in doses in the effort to find the minimum. This long wait was intentional, its object being to avoid any hang-over effect of the large doses previously administered. At the

close of the experiments most birds, particularly those whose body weights had been on the decline for several days, received 1 gram of the vitamin powder and all but one of them showed a definite and immediate response by an increase in body weight. For an illustration of this see the curve for bird 27 in Chart 1.

In Table 2 are presented the data on the vitamin minimum for each bird together with the body weight and length of period over

TABLE 2

Amounts of Vitamin B Concentrate Required by Pigeons of Different Body Weights

BIRD NUMBER	PERIOD OF PRACTICALLY CONSTANT BODY WEIGHT	BODY WEIGHT AVERAGE	VITAMIN PER DAY AVERAGE
	days	*grams*	*mgm.*
40	20	300	40
22	7	310	60
37	18	350	60
25	10	390	120
41	7	410	80
23	13	415	80
30	20	420	85
27	17	420	90
39	14	420	85
42	17	420	90
44	18	440	95
33	30	440	100
39	6	450	100
38	18	465	100
32	10	465	100
31	9	485	130
34	14	500	120
26	42	510	120
48	9	520	120

which the weight remained practically constant. In the case of pigeon 39 the vitamin minima for two quite different body weights were accurately determined. The data pertaining to both of these weights are included in this table. It will be noticed that there is a general increase of the vitamin minimum associated with rise in body weight. Only two birds—no. 25 and no. 31—are exceptional in this respect. It is quite possible that these pigeons had either poorer utilization or greater loss of vitamin through excretory channels than the other birds.

The Vitamin B Minima Considered in Relation to the Body Weights of the Respective Pigeons

If the data on vitamin per day—last column of Table 2—are plotted as ordinates with corresponding body weights as abscissae, the resulting graph suggests that the vitamin minimum is a function of some power of the body weight. An effort was made to determine what this power might be.

Reference has already been made to the possibility that the vitamin B requirement stands in some relation to metabolism (see page 5). Basal metabolism is closely proportional to body surface area, or "active protoplasmic mass" for which surface area may be

TABLE 3

Test of a Proposed Vitamin Formula by Data Obtained from Pigeons

ALGEBRAIC EXPRESSION TESTED	VALUE OF n FIXED AT	CALCULATIONS	
		Mean K	Average deviation in percent of mean
$\frac{VIT}{W^n} = K$	$\frac{1}{3}$	12.1	15.9
	$\frac{2}{3}$	1.60	12.6
	$\frac{3}{3}$	$2.10^{10^{-1}}$	9.7
	$\frac{4}{3}$	$2.78^{10^{-2}}$	6.9
	$\frac{5}{3}$	$3.70^{10^{-3}}$	5.5
	$\frac{6}{3}$	$4.91^{10^{-4}}$	5.8
	$\frac{7}{3}$	$6.55^{10^{-5}}$	7.4
	$\frac{8}{3}$	$8.76^{10^{-6}}$	10.4

taken as a good index, and body surface area is a fairly close function of the two-thirds power of the weight.[1] This suggests that the value $\frac{2}{3}$ might be the desired power. This idea was tested in the manner about to be described, the test being made more rigid by basing the calculations not only on this value but others as well. The data contained in Table 2 for body weight and corresponding vitamin minimum were used to test an expression of the type

$$\frac{\text{Vitamin}}{\text{Weight}^n} = K \tag{1}$$

where n was varied from $\frac{1}{3}$ through $\frac{2}{3}$, $\frac{3}{3}$, $\frac{4}{3}$ . . . up to and including $\frac{8}{3}$. The values of K yielded in each series of calculations based upon

1. For a general discussion of this topic see DuBois: Basal Metabolism in Health and Disease, Lea and Febiger, N. Y., 1924.

a given fixed value of n were compared and the degree of variation noted. Examination of the means and the average deviations from the mean of the respective series indicated what value for n gave the best agreement of values for K and the extent of that agreement.

In Table 3 are presented the results of such calculations. It will be noticed that the best agreement of the values of K is obtained when n is fixed at $\frac{5}{3}$. The average deviation for this series is 5.5 percent of the mean.

The data in Tables 2 and 3 indicate that the adult pigeon's vitamin B requirement in terms of lot 985 of Yeast Vitamin Powder (Harris) can be approximated quite accurately by the expression

$$\text{(2)} \qquad \text{Pigeon: VITAMIN B}_{\text{mgm. per day}} = 0.0037\ \text{WEIGHT}_{\text{gram}}^{\frac{5}{3}}$$

Discussion of this expression will be given later when the data yielded by all the species can be considered.

CHAPTER V

ANIMAL EXPERIMENTS: VITAMIN B (B_1) TESTS WITH THE DOG

THE dog proves to be an excellent animal for studies of the sort described in this monograph because of the ease with which the relation of vitamin B (B_1) to the maintenance of the normal urge to eat may be demonstrated in this species. When such a relationship was first suggested, it was imperative to demonstrate by both positive and negative control experiments that vitamin B was the dietary factor responsible for restoration of the appetite. Numerous substances were assayed for vitamin B on rats. Tests of these same products on the dogs which had lost the urge to eat a vitamin B-deficient ration, showed a similar rating of the assayed materials. In Table 4 these tests are listed and the relative potencies of the different products indicated by plus signs.

It is not intended in Table 4 to convey the idea that an *absolute* correlation exists; that, for example, the brewery yeast, alcoholic extracts of rice polishings and wheat embryo, and the "vitavose" with their "3 plus" signs are of exactly equal vitamin content and appetite-promoting power. So far as the tests showed, these products seemed to be of approximately equal vitamin value, each being much better than the baker's yeast, somewhat better than the tomato suspension, and certainly much less potent than the yeast vitamin powder.

This parallelism suggested an approach to the problem of ascertaining the dog's vitamin B requirement using the restoration and maintenance of the urge to eat as the criterion for the satisfaction of the vitamin need. The availability of yeast vitamin powder (Harris) and vitavose solved the problem of having suitable amounts of materials relatively rich in vitamin B and obtained from two widely different sources, namely yeast and wheat embryo. As a control substance for such experiments commercial beef extract was used; this material does not contain vitamin B (Damon, 1922).

Diets Used in Experiments with Dogs

The experimental diets used with the dogs are shown in Tables 5 and 6. They are constructed according to the kilo-unit plan, which, for each kilogram body-weight of the dog provides so far as possible all the known dietary essentials except the variable of special

TABLE 4

The Vitamin B Values of Different Products Shown by Assays with the Rat and Pigeon Techniques and by Appetite Studies in the Dog

SUBSTANCE TESTED	VITAMIN B CONTENT (RAT AND PIGEON METHODS)	APPETITE-PROMOTING POWER (DOG METHOD)
Yeast, brewery (tested by Karr*)	+++	+++
Yeast, bakers' (tested by Karr*)	+	+
Tomato, suspension of (tested by Karr*)	++	++
Rice polishings, alcoholic extract of	+++	+++
Wheat embryo, alcoholic extract of	+++	+++
Navy bean, alcoholic extract of	+	+
Yeast Vitamin Powder (Harris)†	++++++	++++++
Vitavose‡	+++	+++
Liebig's beef extract, commercial	−	−

* W. G. Karr: 1920.
† From the Harris Laboratories, Tuckahoe, New York.
‡ From the Ward Baking Company, New York.

TABLE 5

Diet III. Artificial Ration Used in Dog Feeding Experiments

	GRAMS	CALORIES	PERCENT
Casein comm'l (12.7% N)	6.3	20.6*	41.2
Sucrose	4.5	18.0	29.4
Lard	2.8	25.2	18.3 } 25.5
Butter	1.1	9.0†	7.2
Bone ash	0.4		2.6
Salt mixture‡	0.2		1.3
Total	15.3	72.8	100.0

This kilo-unit contains 0.8 gram of N, and 73 calories, 46.5 percent of which are furnished by fat.
* Calculated on a basis of 81.9 percent protein.
† Figured as containing 90 percent fat.
‡ Used by Karr (1920).

interest. Examination of Tables 5 and 6 will show that these diets provide ample protein nitrogen, a mineral mixture of desired composition, roughage in the form of bone ash, vitamin A in the form of butter, and calories sufficient for maintenance of animals of the

size used in these studies. The diets as presented in these tables are complete for the dog so far as is known except with respect to the vitamin B complex; for studies of the type here described, vitamin B is provided in the test material fed separately.[1]

Behavior of the Dog Subsisting on a Vitamin B-Deficient Diet

Before proceeding to a presentation of the quantitative data obtained with the dog, it seems worth while to describe the behavior of members of this species when restricted to such rations as are described in Tables 5 and 6. Such a description will assist the

TABLE 6

Diet IV. Artificial Ration Used in Dog Feeding Experiments

	GRAMS	CALORIES*	PERCENT
Meat residue† (13 percent N)	6.15	21.6	37.3
Meat residue† (10 percent fat)		5.67	
Sucrose	5.63	23.5	34.1
Lard	3.00	28.4	18.2
Butter	1.12	9.46‡	6.7
Bone ash	0.4		2.5
Salt mixture§	0.2		1.2
Total	16.50	88.6	100.0

This kilo-unit contains 0.8 gram of protein N. One gram of this food mixture contains 5.68 calories.

* Loewy's factors are used, namely, 4.32 for protein, 4.18 for carbohydrate, and 9.46 for fat.

† From the Valentine Meat Juice Company, Richmond, Virginia.

‡ A 10 percent correction for salt and water content.

§ Used by Karr (1920).

reader in understanding more clearly why we believe the disease beriberi in humans to involve fundamentally a lack of vitamin B.

Anorexia

At the beginning little or no difficulty is experienced in making dogs eat the food offered. As Karr (1920) had pointed out pre-

1. When the dog receives sufficient amount of vitamin B, he will eat a constant daily quantity of an artificial ration of the type presented in Tables 5 and 6. This fact is of great significance to students of metabolism and nutrition. Review of the experimental work in the field of metabolism indicates many studies which met with great difficulty and often complete failure, because after a period the dog refused to eat the experimental ration. It is not our purpose to discuss here this interesting application of the findings of vitamin B research. The reader who wishes to pursue this topic will find it discussed in some detail by the author in the *Journal of Biological Chemistry, Vol.* 56, p. 725, July, 1923.

viously, however, we have found that the animals, after having been fed on the vitamin-free food for a short time, differ as to the amounts of the food which they will eat daily. A loss of appetite soon reveals itself resulting in a lowered and irregular food intake

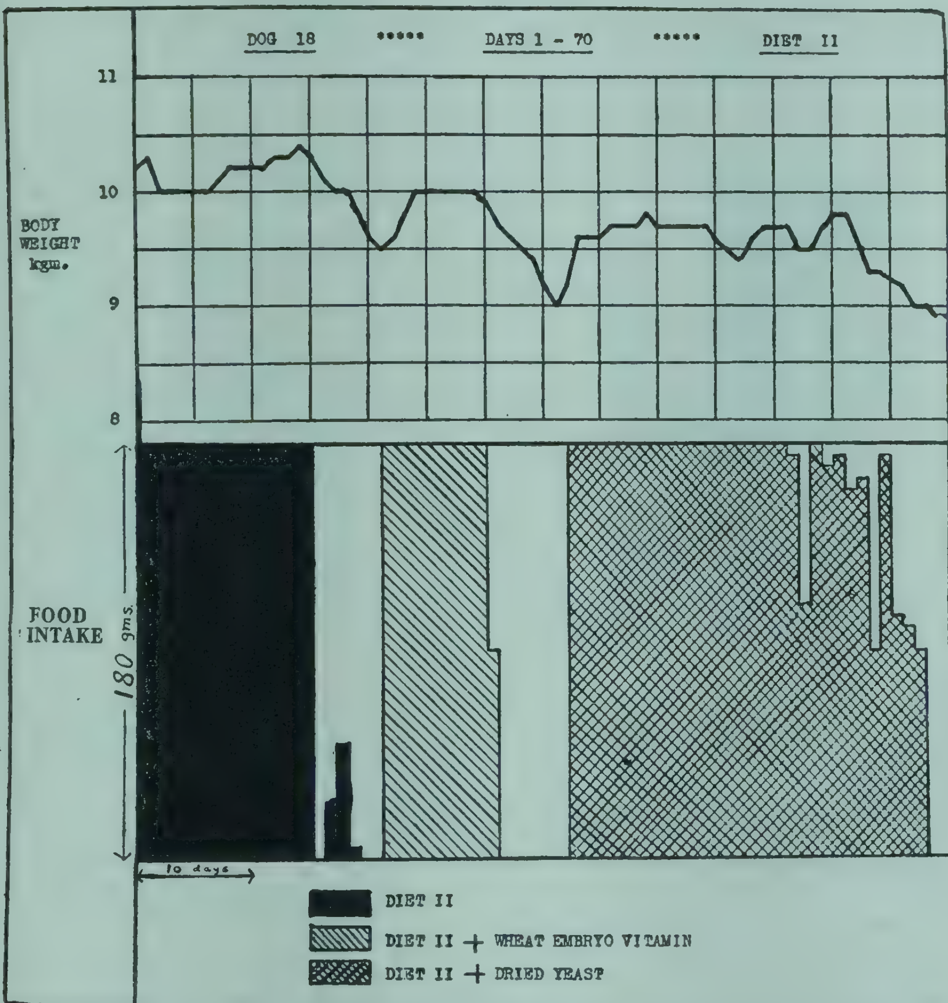

CHART 2

Illustration of the Effect of Vitamin B (B_1) Administration on the Anorexia Due to Lack of This Dietary Factor in the Dog. This graph is based on the data obtained from dog No. 18.

and occasionally in a complete refusal of the food over many days. We have gained the impression that if the animal continues to eat *some* food every day, it more readily develops symptoms of polyneuritis.

It is obvious that failure of the animal to eat a sufficient amount of food must result in loss in body weight. In Chart 2 are plotted food intake and body weight data yielded by dog 18. The maximum ordinate represents the amount of food offered daily; the amount of food actually eaten is indicated by the height of the black column. On the nineteenth and twentieth day the refusal of food was absolute. During the afternoon of the twentieth day an extract of wheat

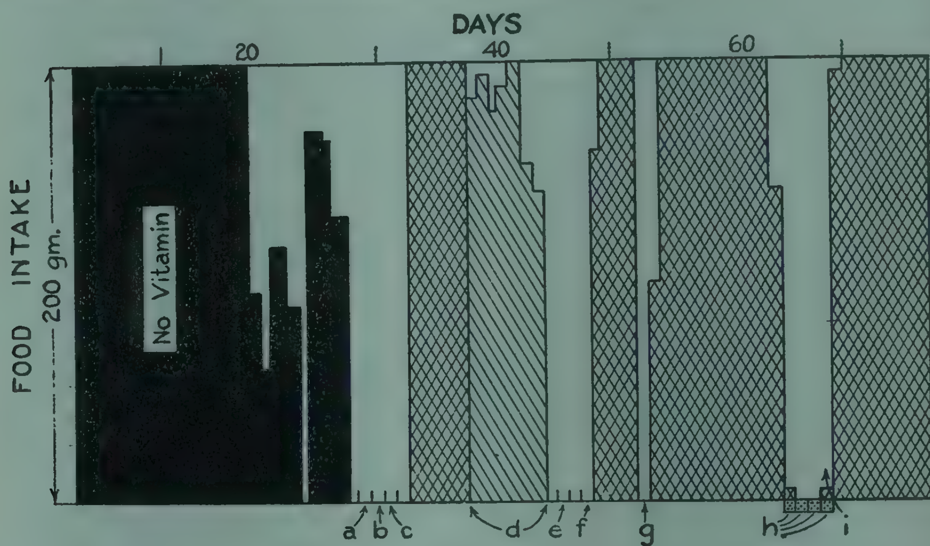

CHART 3

The Negative Effect of Administration of Beef Extract, a Substance Devoid of Vitamin B (B_1), on the Anorexia Due to Lack of This Dietary Factor in the Dog. In these experiments with Dog 39 notice that neither the administration of large doses of the commercial material, *a*, nor the mixing of it with the food, *h*, influenced the appetite favorably. The graded responses to vitamin B (B_1) administration, as shown by the number of days over which the appetite was restored, are evident at *c*, *f* and *g*. The doses given at *b* and *e* were evidently subminimal. *Intravenous* injection of this vitamin preparation, *i*, was also effective in restoring the appetite.

embryo was administered by stomach tube. On the following morning, and for nine days following, all the food offered was eaten within a few minutes. The vitamin was administered by stomach tube for two reasons: first, to make certain that the animal received it; and second, to guard against the possibility that change in the taste of the ration might be responsible for the restoration of the appetite.

It will be noticed that dog 18 (Chart 2) after eating well until

the thirty-first day, again exhibited complete anorexia for six days. This was finally corrected by the administration of dried brewery yeast by stomach tube with the result that perfect appetite was maintained for eighteen days, after which a partial loss of the urge to eat again manifested itself.

The results of control experiments with beef extract support the view that vitamin B is the dietary factor responsible for correction of this interesting anorexia. Experiments illustrating this point are shown graphically in Chart 3.

Neither the administration of single large doses of commercial beef extract—*a*—nor the mixing of it with food—*h*—influenced the appetite favorably. The graded responses to vitamin administration as shown by the number of days over which the appetite was restored, are evident at *c*, *f* and *g*. The doses given at *b* and *e* were evidently subminimal. Intravenous injection of this vitamin preparation, *i*, was also effective in restoring the urge to eat.

Neuromuscular Manifestations: Polyneuritis

If the dog continues to eat appreciable amounts of the vitamin-free ration over a sufficiently long period, neuromuscular manifestations of vitamin B deficiency develop. Uusually, but not always, vomiting is the first symptom noted. At this time a foul breath is usually present. Some animals exhibit convulsive seizures, in which all limbs are extended, as, for example, in Fig. 5. This may result in sudden death, or may be repeated at intervals for as long as about twenty-four hours, finally disappearing after administration of sufficient amount of vitamin B by stomach or parenterally. Fig. 6 shows the same animal as in Fig. 5, 18 hours later, after having received large doses of tomato juice by mouth. Figures 7 and 8 are photographs of a dog taken during a convulsive seizure, and four hours later, after the animal had received an intravenous injection of vitamin B concentrate. Following this treatment the muscles were relaxed, and the animal no longer exhibited clonic spasms when handled; the dog was able to walk, the only manifestation of vitamin B deficiency now apparent being a moderate spasticity of the muscles of the hind limb resulting in a spastic gait.

Sometimes the dogs show a gradually developing spastic paralysis which is remarkably like the picture of beriberi. Facing page 18

are two photographs of such an animal, (Figs. 3 and 4) which should be compared with the picture illustrative of human beriberi (Fig. 2) taken from Bältz and Miura. (See page facing p. 12.) The fact that both of these syndromes, that appearing in the dog and the disease developing in the human species, are cured promptly following administration of sufficient amounts of vitamin B, makes it quite evident that careful study of the experimentally-produced condition, both qualitatively and quantitatively, promises much of value for the human species.

Vitamin B Minima of Dogs

In our first quantitative tests with the dog, we studied the effect of administering single doses of the yeast vitamin powder (Harris) and the wheat germ preparation vitavose. The results were sufficiently uniform to indicate that a definite relationship exists between the amount of the vitamin administered, size of the animal in terms of body weight, and the number of days over which the appetite would be maintained perfectly. It was then thought that the daily vitamin B minimum might be slightly lower if the dietary essential were given daily. There was the possibility that tests with single doses of the vitamin-containing product are likely to be made on animals whose conditions of vitamin B deficiency are not the same, and therefore not strictly comparable. Consequently definite daily doses of the preparations were given and the periods over which the urge to eat could be successfully maintained, were made the criteria as to the satisfaction of the dog's requirement for vitamin B.

In 1923, Cowgill and Deuel reported concerning these experiments and stated that "dogs require approximately 40 mgm. of the yeast vitamin powder (Harris) per kilogram body weight per day to maintain perfect appetite over periods of several months duration." These experiments were described in detail in a later paper by Cowgill, Deuel and Smith (1925). The tests with single doses of the powder had indicated that from 50 to 60 mgm. per kilogram per day represented the vitamin B minimum of dogs. Daily doses of 20, 30, 40, 50 and 60 mgm. were then given daily over long periods. In every case where the 20 mgm. was tested there was failure of the appetite after from fifteen to thirty days;

FIG. 5

Extreme Vitamin B (B_1) Deficiency in the Dog. This animal subsisted on the diet shown in Table 5, which is deficient in vitamin B (B_1). The leg muscles were vigorously contracted, especially those of the hinder extremities, resulting in extension of all the limbs and inability of the animal to stand. If this dog was handled, severe clonic spasms resulted. (Photograph reproduced through the courtesy of the *American Journal of Physiology.*)

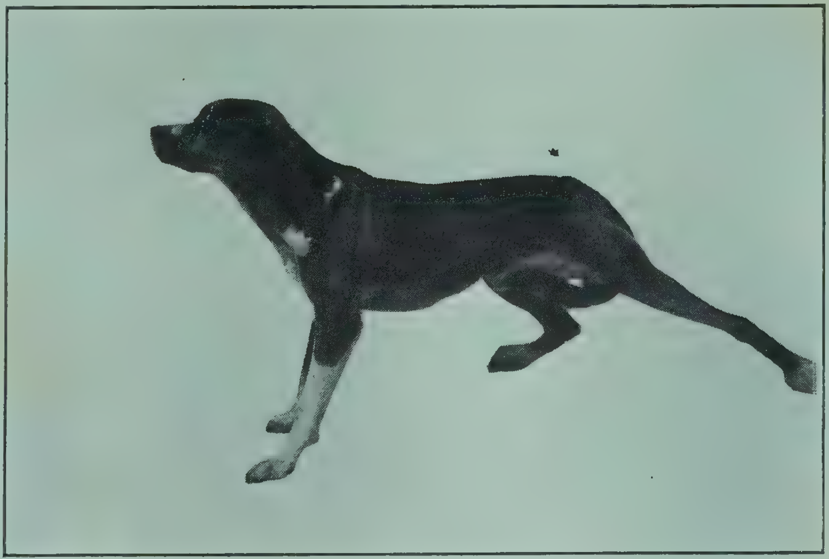

FIG. 6

Same Dog as Shown in Fig. 5, Photographed 18 Hours After Receiving Vitamin B (B_1) in the Form of Neutralized Tomato Juice. As a result of this treatment the animal was able to stand and to walk although with a characteristic spastic or "steppage" gait. After repeated treatments extending over four days, the spasticity of the leg muscles and spastic gait almost entirely disappeared. (Photograph reproduced through the courtesy of the *American Journal of Physiology.*)

the 30 mgm. dose was insufficient in one case but adequate in another; in every instance where the 40, 50 and 60 mgm. doses were given there was perfect maintenance of the urge to eat for at least three months. On the basis of these observations it was concluded that about 40 mgm. per kilogram per day represented the vitamin B minimum of the dog.

Inasmuch as these tests required much time for their proper performance and the supply of lot 985 of the vitamin concentrate was rapidly diminishing, it was deemed advisable to pursue the problem further with other species of animals rather than to repeat and extend the work done with the dog. Our pigeon data, obtained later, indicated that it might be worthwhile to review the dog data,

TABLE 7

The Amounts of Vitamin B Concentrate Required by Dogs of Different Body Weights

DOG NUMBER	BODY WEIGHT*	VITAMIN CONCENTRATE PER DAY*
	grams	*mgm.*
44	4,550	90
45	6,000	165
41	8,000	232
55	9,850	360
53	10,000	360
39	11,000	384

* Body weights and vitamin dosages are expressed in grams and milligrams respectively because these units are used with the other species studied.

paying particular attention to the body weight and vitamin dosage of each animal. This was done. In Table 7 are given the daily intakes of vitamin powder for six dogs ranging from 4.5 to 11 kilograms body weight. In every case the behavior of the animal at the end of a period of at least three months was such as to indicate that its vitamin intake was *very close* to the minimum required. Certainly very little excess vitamin was being ingested daily. This is a very important point worthy of emphasis. Many other dogs were experimented with but the data yielded by them cannot be considered here because the animals were undoubtedly receiving a considerable excess of vitamin above the minimum required for physiological well being.

Following the hint given by the results of the pigeon experi-

ments, the data contained in Table 7 were examined to see how well they fit the expression

$$\text{(1)} \qquad \frac{\text{Vitamin}}{\text{Weight}^n} = K$$

and an effort made to determine the value of n that gives the best agreement of the values of K by varying n through $\frac{1}{3}$, $\frac{2}{3}$, $\frac{3}{3}$, etc., as was done with the data for the pigeons. The results of the calculations are presented in Table 8.

Examination of Table 8 shows that there is the least variation in values of K when the exponent of the weight is $\frac{5}{3}$. The average

TABLE 8

Test of a Proposed Vitamin Formula by Data Obtained from Dogs

DOG NUMBER	$\frac{\text{VITAMIN}}{\text{WEIGHT}^n} = \text{K}$							
	$n = \frac{1}{3}$	$\frac{2}{3}$	1	$\frac{4}{3}$	$\frac{5}{3}$	2	$\frac{7}{3}$	$\frac{8}{3}$
		10^{-1}	10^{-2}	10^{-3}	10^{-5}	10^{-6}	10^{-7}	10^{-8}
44	5.43	3.28	1.98	1.25	7.21	4.35	2.63	1.58
45	9.08	5.00	2.75	1.51	8.33	4.58	2.52	1.39
41	11.60	5.80	2.90	1.45	7.25	3.68	1.81	0.91
55	16.80	7.84	3.66	1.71	7.76	3.71	1.73	0.81
53	16.71	7.76	3.60	1.67	7.96	3.60	1.67	0.78
39	17.30	7.76	3.49	1.57	7.06	3.17	1.43	0.64
Mean	12.82	6.24	3.06	1.52	7.60	3.84	1.97	1.03
Average deviation	4.11	1.55	0.52	0.12	0.42	0.42	0.41	0.31
Average deviation in percent of mean	32.1	24.8	17.0	7.90	5.53	10.9	20.8	30.1

deviation in per cent of the mean in this case is ± 5.53, which is almost identical with that for the pigeons, namely, ± 5.5 (see Table 3). From the data presented in Tables 7 and 8 it appears that the adult dog's daily vitamin B requirement in terms of lot 985 of the yeast vitamin powder (Harris) may be approximated quite accurately by the expression

$$\text{(3)} \qquad \text{Dog: VITAMIN B}_{\text{mgm. powder per day}} = 0.000076 \ \text{WEIGHT}^{\frac{5}{3}}_{\text{gram}}$$

Comparison of this expression with that obtained for the pigeon reveals a striking similarity. Discussion of this formula will be deferred until all of the data for the several species have been presented (see Chapter VII).

CHAPTER VI

ANIMAL EXPERIMENTS: VITAMIN B (B_1) TESTS WITH THE WHITE RAT AND MOUSE

Critique

ENTIRELY satisfactory experiments designed to determine the amounts of vitamin B just sufficient to allow physiological well being in rats of different sizes are not easy to plan. Osborne and Mendel (1922) gave different groups of young rats definite constant amounts of dried yeast as the source of vitamin B over a period of approximately a year and compared the rates of growth exhibited by the several groups of animals. Small doses limited growth to a marked extent; larger doses were associated with growth somewhat below normal and approximately the same as that usually obtained on complete rations of the type used. Sherman and Spohn (1923) utilized this scheme in developing their method of biological assay of foods for vitamin B.

Although such a plan of experimentation yields valuable data and serves to demonstrate in striking fashion how the intake of vitamin B may be a limiting factor in growth, in our opinion it cannot give data that can be compared satisfactorily with those obtained from the pigeon or the dog. Consider the rats to which Osborne and Mendel gave a daily dose of 25 mgm. of dried yeast. It took over seven months for any of these animals to attain a weight approximating 180 grams. Is it permissible to regard animals that have endured such a repression of growth as "normal" or justly to be compared with others that have not been so repressed? It is doubtful if this question can be answered at all satisfactorily, in view of the present state of knowledge. Mere mention of it, however, serves to emphasize at least one point to be considered in planning the quantitative experiments useful in attaining the main objective of this research, namely, that the experimental conditions under which the vitamin B minimum is to be measured should be such as to allow the animals to be in a condition as nearly normal as possible.

There is also the question as to whether the vitamin B requirement for maintenance of animals at a specified weight is the same or much less than the amount needed to permit growth in addition to maintenance. In all probability, judging from various facts already known concerning the dietary cost of growth as compared with maintenance, it is quite likely that more vitamin B is required to permit increase in size than that needed to maintain the organism at a given weight. Just what the quantitative relationship between these particular vitamin B minima may be, however, remains for further research to determine.

Another point that must be considered in planning work of the sort discussed in this chapter concerns the vitamin B demonstrated to be present in the intestinal excreta. The experiments of Osborne and Mendel referred to above were not conducted under conditions where ingestion of the feces by the test animals was prevented. When a preliminary report of our work (Cowgill and Deuel, 1923) was given, showing that the young rat's requirement for vitamin B per unit of body weight is approximately five times that of the dog, the communication dealt with rat experiments in which coprophagy was possible. After our experiments had been completed there appeared the paper of Steenbock, Sell and Nelson (1923) calling attention to the vitamin B present in the feces and emphasizing the importance of considering this source of supply when performing quantitative vitamin B tests on animals. Their observations were soon confirmed not only in our own laboratory (Smith, Cowgill and Croll, 1925) but elsewhere (Dutcher and Francis, 1923–24). Our quantitative studies on the rat were therefore repeated with the experimental animals housed in specially constructed false-bottom cages described by Smith, Cowgill and Croll (1925).

Plan of Experiments

Young rats of approximately 60 grams body weight were allowed to subsist on a vitamin B-free ration consisting of 18 percent extracted casein, 51 percent corn starch, 18 percent lard, 9 percent butter fat and 4 percent Osborne-Mendel (1917) salt mixture. Each animal received daily a carefully weighed amount of the lot 985 Yeast Vitamin Powder (Harris). This material was weighed on a tared crucible cover, the handle of which had been removed in

order to make the cover lie flat. The error in weighing the vitamin powder was not over 0.5 mgm. The growth of the animal was followed carefully, weighings being made twice a week. When two consecutive records indicated a definite decrease in the growth rate, the daily dose of vitamin powder was increased by a fixed measured amount. When the growth rate again showed a decline, the amount of vitamin was increased once more.

One advantage of this procedure lies in the fact that the animals are not allowed to become seriously ill, nor are they forced to endure a marked suppression of growth. This technique has one serious disadvantage. It is often quite difficult, in some cases impossible, to determine just when the growth rate begins to decrease. The break or change in the graph cannot be definitely fixed. The only way this difficulty can be circumvented seems to be to perform a number of experiments sufficiently large to allow one to disregard the doubtful cases.

It was reasoned that the decrease in the growth rate was due in the first instance to failure to eat an amount of food sufficient to permit normal growth, and the failure to eat was due to a lack of vitamin B. In other words, appearance of the anorexia characteristic of vitamin B deficiency is the criterion that the need for this vitamin is not being met. Inasmuch as the failure to maintain growth was exhibited over a relatively short period, the condition of the animal could not be regarded as differing seriously from the "normal."

It is possible to take the view that in these experiments performed in 1923, the decrease in growth rate was due to an insufficient supply of the heat-stable pellagra-preventive substance, rather than to a shortage of vitamin B. As indirect evidence against this view we may cite (*a*) the observations of Sherman and Sandels (1929) that the "antipellagra" factor is difficult to extract from commercial casein, the source of protein fed by us, by means of varying concentrations of ethyl alcohol, and (*b*) the finding (Cowgill, Rosenberg and Rogoff, 1931; Burack and Cowgill, 1931; Sherman and Sandels, 1931) that the loss of appetite characteristic of a shortage of the vitamin B complex is to be attributed to lack of the antineuritic B factor and not the "pellagra-preventive" vitamin G. It is likely, therefore, that our extracted casein con-

tained appreciable amounts of the heat-stable G vitamin. Inasmuch as the first indication of change in the growth rate is the sign looked for, and this is a prompt result of anorexia, it is considered more likely that the data obtained with these rats pertain to the antineuritic vitamin B.

Data Yielded by Rat Experiments

The first set of experiments was performed with a group of eleven rats (Nos. 42 to 53 inclusive, Table 9). These animals were used only to determine the body weight to which young rats might go when given 20 mgm. of the vitamin powder per day. It was the behavior of these animals and a study of their growth curves that suggested the idea underlying the technique described above. These rats showed considerable variation with respect to the body weight levels at which the growth rate changed and at which the vitamin dosage had to be increased. Partly to increase the number of observations and partly to determine whether, on the basis of the experience now gained, the accuracy might not be increased and the variation thus diminished, another group of nine animals was started. The mean body weight for the 20-mgm. dose and the average deviations in percent of the mean for the two series of experiments proved to be almost identical. From this it was concluded that further experimentation using this technique with the view to decreasing the average variation by increasing the number of cases was not worth while.

Data were secured from a total of 20 rats given 20 mgm. of the vitamin concentrate per day until a definite change in growth rate occurred, then given 30 mgm. and lastly 45 mgm. per day. It proved possible with all the rats to fix with reasonable accuracy the body weight at which growth began to decrease when the animals were given the 20-mgm. dose; in six cases the point was fixed for the 30-mgm. dose, and in four cases for the 45-mgm. daily allowance of yeast concentrate, making a total of 30 cases available for study. The data are presented in Table 9.

The 30 cases listed in Table 9 were examined with the view to determining the best value for the exponent of the body weight in the expression similarly tested on pigeons and dogs. The average body weights for the different vitamin doses were also used for

TABLE 9

The Amounts of Vitamin B Concentrate Required by Rats at Different Body Weights

RAT	YEAST VITAMIN CONCENTRATE DOSAGE OF 20 mgm. per day	30 mgm. per day	45 mgm. per day
	Body weight reached		
	grams	*grams*	*grams*
856	108	143	158
857	104	149	?
855	103	?	136
852	102	126	?
859	101	132	?
854	94	118	?
858	92	?	128
860	88	126	148
853	87	?	?
44	110		
42	108		
43	106		
45	102		
53	101		
52	100		
51	95		
48	92		
46	90		
49	86		
47	80		
Total cases..........	20	6	4
Average weight.......	98	132	143
Average deviation in percent of mean.....	7.1	5.5	7.3

TABLE 10

Test of a Proposed Vitamin Formula by Data Obtained from Rats

ALGEBRAIC EXPRESSION TESTED	VALUE OF n FIXED AT	CALCULATIONS BASED ON ALL 30 CASES: Mean K	Average deviation in percent of mean	CALCULATIONS BASED ON AVERAGE WEIGHTS FOR EACH GROUP: Mean K	Average deviation in percent of mean
$\frac{\mathrm{VIT}}{\mathrm{W}^n} = K$	$\frac{1}{3}$	5.2	22.4	6.3	24.5
	$\frac{2}{3}$	1.1	17.0	1.3	21.6
	$\frac{3}{3}$	2.3^{10-1}	13.6	2.5^{10-1}	18.4
	$\frac{4}{3}$	4.7^{10-2}	12.7	5.0^{10-2}	14.0
	$\frac{5}{3}$	9.9^{10-3}	13.0	9.9^{10-3}	9.0
	$\frac{6}{3}$	2.1^{10-3}	15.9	2.0^{10-3}	10.0
	$\frac{7}{3}$	4.4^{10-4}	19.6	4.0^{10-4}	10.8
	$\frac{8}{3}$	9.0^{10-5}	22.2	8.2^{10-5}	13.0

such a test. The results of these calculations are presented in Table 10.

In the calculations (Table 10) based on all 30 cases, it will be noticed that the best value for n, as shown by the minimum average deviation, is $\frac{4}{3}$, and that the average deviation in percent of the mean in this case is only very slightly lower than that obtained when n is $\frac{5}{3}$. If the average body weight values for the three vitamin dosages are used for the calculations (last two columns of Table 10) $\frac{5}{3}$ is clearly indicated as the best value for n, giving an average deviation of 9 percent of the mean value of K which is 0.0099. The following expression may therefore be formulated:

$$\text{(4)} \qquad \text{Rat: VITAMIN}_{\text{mgm. per day}} = 0.0099 \ \text{WEIGHT}^{\frac{5}{3}}_{\text{gram}}$$

This expression is obviously applicable to rats ranging from 80 to 160 grams body weight with an accuracy of about 9 percent. Upon initial consideration this may appear to be too great a variation. It is pertinent, therefore, to call attention to the fact that this is only slightly greater than the variation in the basal rate of metabolism exhibited by normal individuals. For example, Harris and Benedict (1919) have shown that the average basal heat production of 104 women is 850 calories per square meter of body surface per day; the average deviation is 7 percent of this mean. In view of these considerations it appears safe to conclude that even these rat data are of significance, particularly when they point to the same type of relationship existing between body weight and vitamin B minimum as is demonstrated to occur with the pigeon and the dog. It is our belief that formula (4) constitutes a closer approach to a true mathematical statement of the rat's vitamin B requirement than first approximation expressions of the type offered earlier, for example, by Osborne and Mendel (1922), where the requirement is stated as "milligrams of yeast per 100 grams of rat."

Data Yielded by Experiments with Mice

When Beard (1925–26a) was studying the nutritive requirements of mice in this laboratory, it was suggested that he endeavor to determine the minimum amount of our lot 985 Yeast Vitamin Powder (Harris) required to allow growth in mice, using the technique previously employed on rats and described above. He en-

countered considerable difficulty in his experiments and was forced to repeat many feeding trials with new groups of animals. Eight instances were finally obtained where the body weights, to which mice could go on a given vitamin dosage before suffering serious repression of growth, were observed. Any error involved in these studies was undoubtedly on the positive side; that is to say, that insofar as the minimum amount of vitamin was only approximated, the quantity given the animals was definitely greater rather than less than the absolute minimum.

When applied to the vitamin expression tested above for the other species, the data for the mice indicate the value of the exponent of the weight to be $\frac{7}{3}$ instead of $\frac{5}{3}$. In view of the fact that the error was undoubtedly on the positive side, this result might be expected. It is our belief that the error of the work on the mice is greater than that for any of the other species, and that before one definitely concludes that mice do not conform to the relationship between body weight and vitamin B minimum found to hold in the other three species studied, further experiments should be performed. Inasmuch as our supply of lot 985 of the yeast concentrate is exhausted, such additional experiments will have to be made with other material. The data yielded by the experiments with mice are shown in Table 11.

TABLE 11

The Amounts of Vitamin B Concentrate Required by Mice at Different Body Weights

YEAST VITAMIN CONCENTRATE PER DAY	BODY WEIGHT AT WHICH THIS AMOUNT OF VITAMIN IS THE MINIMUM
mgm.	*grams*
10	14
10	14
20	20
20	19
30	23
30	23
40	26
40	26

CHAPTER VII

COMPARISON OF DATA YIELDED BY DIFFERENT ANIMAL SPECIES

The Species Constant

FROM the data presented in the previous three chapters it is evident that the same formula, except for the equating constant, can be used to express the need for vitamin B. This vitamin requirement is in linear relation to the $\frac{5}{3}$ power of the body weight. A comparison of the several formulae shows that the value of the equating constant K_s (*species constant*) is greatest for the smallest species and varies inversely with species size. For example:

$$\text{VIT} = K_s \cdot W^{\frac{5}{3}} \tag{5}$$

where

$$K_{\text{rat}} = 0.0099 \text{ or about } 0.01 \tag{6}$$

$$K_{\text{pigeon}} = 0.0037 \tag{7}$$

and

$$K_{\text{dog}} = 0.000076 \tag{8}$$

If it be assumed that this expression is a fundamental one and that its failure with the mouse is due to greater difficulty of experimentation with this species, one can estimate from the mouse data at hand that

$$K_{\text{mouse}} = 0.15 \text{ approximately} \tag{9}$$

A plot of all the data for all species on the same paper gives an interesting graph shown in Chart 4. Because the values for body weight cover so wide a range, from a 14-gram mouse to an 11,000-gram dog, the logarithms of the body weights are plotted as abscissae against the logarithms of vitamin requirements as ordi-

nates. The slopes of the plots for the individual species seem to point to a common origin, which was finally fixed more or less arbitrarily as the point -2.75 on the ordinate or y axis. The slants for the rats, pigeons and dogs agree well with such a plot; the slope for the mice does not conform so well.

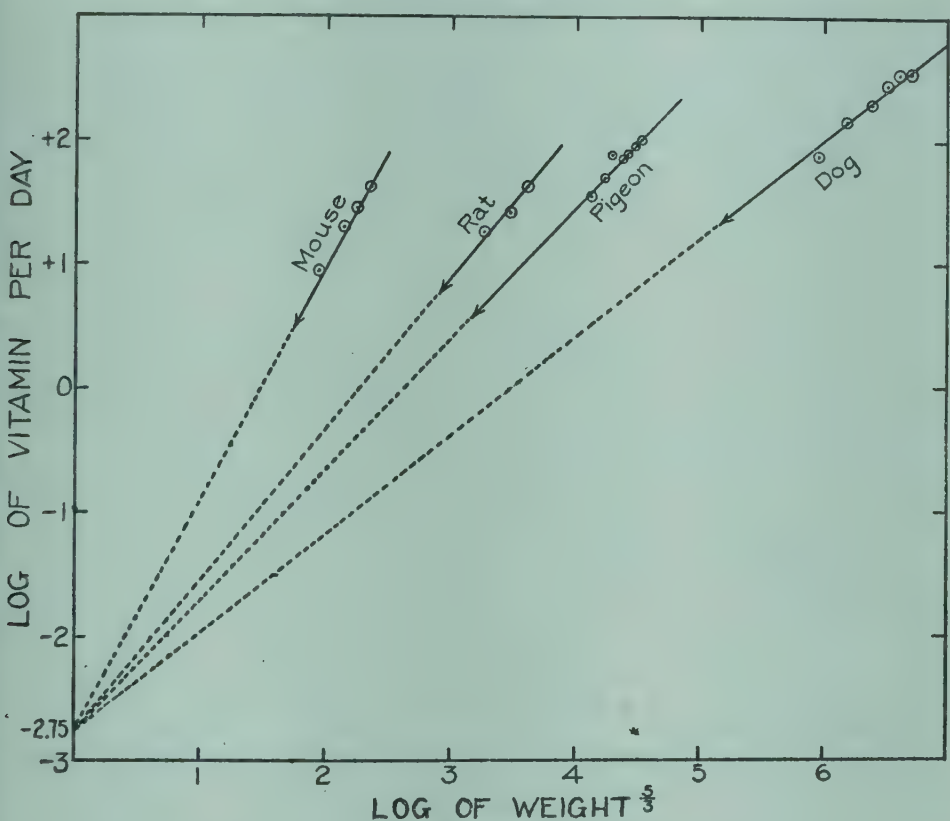

CHART 4

Vitamin B (B_1) Minima in Relation to Body Weight in the Four Species Studied. When the vitamin B (B_1) minima and five third powers of the body weights for all the species are plotted on the same paper, logarithms of the two variables being used because of the extremely wide range of values to be plotted, the graph shown in Chart 4 is obtained. The lines for the respective species point to a common origin on the y axis indicating the existence of a constant common to all of these species which is represented mathematically by the value of the intercept 0 to -2.75 on the y axis.

Inspection of Chart 4 indicates the existence of a constant common to all of the species, namely, the intercept of -2.75 on the *log vitamin* axis; the values of the slopes for the various species are,

of course, the ratios of this common slant, -2.75, to the respective intercepts on the *log Weight*$^{\frac{5}{3}}$ or x axis, and are peculiar to each species. From Chart 4, by elimination of logarithms, one obtains an expression of the following type:

$$\text{VIT} = K_u \cdot (W_i^{\frac{5}{3}})^{k_s} \tag{10}$$

where VIT signifies vitamin per day, K_u is the common or universal (?) constant, W_i is the body weight of the individual in question, and k_s is a constant, the value of which is peculiar to the species. Expression 10, although interesting in its suggestion that there is some factor common to all of these species, does not prove immediately applicable in the solution of the main problem of this research.

Considerable effort was expended in an endeavor to relate the species constant to the size of certain organs, systems of organs, and other variables which conceivably should vary appreciably in different species. Numerous interesting data relating to fractions of body weight represented by organs, etc., were collected, but no relationships by which to explain the differences in species vitamin constant were discovered.

Maximum Normal Weight as a Factor

The problem was then attacked from another point of view. The fact that the species constant varies inversely with size of the species raised the question as to what might be the limiting value of the species size in this connection. Would a plot of what might be called the *maximum normal weight for the species* against species vitamin constant be indicative of any relationship of value? This point of view has something more than mere speculation to support it. It is obvious that if a comparison of individuals of different species is to be made on any weight basis, the individuals must be of comparable ages, or in physiologically equal stages of development; just how one might determine what would be comparable ages or stages of development for the individuals of the species under investigation is not clear. Suppose, however, that the *maximum normal weight* for each species be taken as the basis upon which to make a comparison. Such a comparison would be made at

what might be regarded as a limiting condition. The individuals representing this limiting condition would be as comparable in physiological stage of development as any others that could be taken. By the term *maximum normal weight* the writer means, not the greatest weight ever found for the species, but the average of the weights of numerous unusually large but normal individuals of the species. Extremely large individuals who represent interesting manifestations of endocrine gland activity are to be regarded as abnormal so far as the present discussion is concerned. Approaching our problem from this point of view let us now inquire as to what may be taken as the *maximum* normal weights for the species here studied.

Beard (1925–26b) cited as the largest mice produced in his colony, individuals weighing 34 grams; larger normal mice have not been reported in the literature so far as the writer has been able to ascertain. Let us therefore take 34 grams as the maximum normal weight of the mouse to use in making our species comparison.

With respect to the rat, Osborne and Mendel (1926) have shown that when suitable diets are employed, individuals of this species can exhibit much more rapid growth rates and attain greater size than those observed previously. This has been confirmed by Smith and Bing (1928). Outhouse (1931) has shown that these rapidly growing animals have normal proportions of bodily parts and therefore are not pathological. In his studies of the velocity constant of growth, Brody (1928) used data furnished by Osborne and Mendel. The maximum body weight shown in Brody's (1928) chart is slightly greater than 520 grams. This figure has therefore been taken as the maximum normal weight of the rat species.

According to Dr. Stanley C. Ball,[1] the maximum normal weight characteristic of pigeons is about three pounds or 1353 grams. In the exhibit at the Peabody Museum of Yale University the largest pigeons are designated as having this weight. The writer has therefore taken 1350 grams as the maximum normal weight for the pigeon species.

Whitney (1927) has collected a large amount of data pertaining to the weights of different breeds of dog. The average of the maxi-

1. Curator of Zoology, Peabody Museum, Yale University.

mum weights for the five giant breeds, Great Danes, Newfoundlands, Mastiffs, St. Bernards and Irish Wolfhounds was found to be 159 pounds or approximately 72 kgm. This figure therefore was taken as the maximum weight for the dog to be used in the comparison of species.

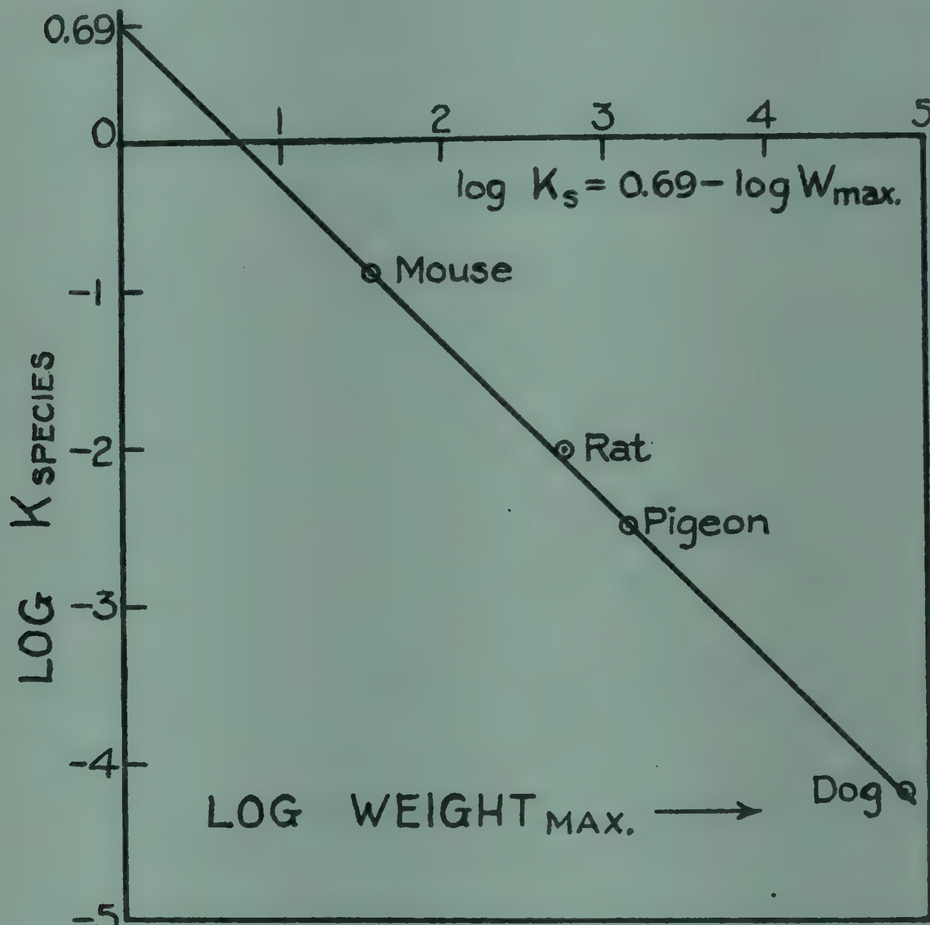

CHART 5

The Inverse Relation between the Species Vitamin Constant and the Maximum Normal Weight of the Species. From this graph it is apparent that the value of the species vitamin constant in the expression VITAMIN = $K_{vit} \cdot WEIGHT^{\frac{5}{3}}$ is inversely proportional to the maximum normal weight characteristic of the species.

Formula Applicable to All Species

The result of a comparison of the vitamin constants for these species (expressions 6, 7, 8 and 9) with the maximum normal weights for the respective species is shown in Chart 5 where $log K_s$

is plotted on the ordinate axis against $logW_{max}$ as the abscissa. Consideration[1] of the plot in Chart 5 leads to the expression:

$$\text{VIT} = \frac{4.9}{W_{max}} \cdot W_i^{1.66} \tag{11}$$

By writing expression 11 as given in formula 12 one obtains some simplification aiding in interpretation.

$$\text{VIT} = 4.9 \cdot W_i^{0.66} \cdot \frac{W_i}{W_{max}} \tag{12}$$

Expression 12, when tested with the experimental data for the several species, yields the calculated vitamin requirements given in the last column of Table 12. These should be compared with the values observed experimentally presented in the adjacent column.

Considering the nature of the experimental work, particularly the difficulties encountered, the agreement of these calculated values with those observed experimentally is excellent. The greatest differences noticed are with the mice, where the error of experimentation was undoubtedly the greatest, and two pigeons and two dogs which required appreciably more vitamin than that estimated by this formula. The latter cases may be instances of individuals that have poorer utilization or storage or greater elimination of the vitamin than most cases. Minot (1929) has emphasized variability of gastroenteric function as a possible cause of variations exhibited by clinical cases in this respect.

In expression 12, the term $W_i^{0.66}$ may be regarded as indicating *metabolism,* because, as is well known, the basal metabolic rate and the body surface area are functions of the two-thirds power of the body weight. The expression $\frac{W_i}{W_{max}}$, the ratio of the individual's weight to the maximum normal or limiting weight for his

1. It will be noticed in chart 5 that through the plots for the various species a line may be drawn cutting the two axes at an angle of 45°. This line intercepts the y axis at point 0.69. From this it is evident that

$$\log K_s = 0.69 - \log W_{max} \tag{13}$$

From the data for the several species it has already been shown that

$$\text{VIT} = K_s \cdot W_i^{1.66} \tag{14}$$

species, stands in some relation to age and growth; in fact, it is one indication of the growth already attained. As the individual grows the value of this ratio approaches unity as a limit. When the value of this ratio is unity, obviously, from the remainder of the formula, the daily vitamin requirement is then dependent entirely upon the metabolism (or some unknown variable which is a function of the two-thirds power of the weight). In the case of the individual who stops growing at some weight below the maximum normal weight for his species, obviously the value of the ratio $\frac{W_i}{W_{max}}$ becomes fixed; the vitamin requirement is then determined by the metabolism (or whatever the $W_i^{0.66}$ signifies) multiplied by a slightly different constant which in this case is the product of 4.9 and the constant value of the ratio $\frac{W_i}{W_{max}}$.

The significance of the ratio $\frac{W_i}{W_{max}}$ as a factor probably related to growth is enhanced when one considers the growth formula that Brody[1] (1927) has brought forward based upon the relation of the body weight to age and to what he calls the *mature weight.* This *mature weight* is somewhat analogous to our *maximum normal weight.* The left-hand part of Brody's formula is similar to our ratio $\frac{W_i}{W_{max}}$ given in expression 12. If, in formula 12 therefore, one were to consider this ratio as indicative of age or growth, expression 12 might be regarded as meaning that the daily vitamin requirement is directly proportional to the *metabolism* of the organism (or some factor which is a close function of the two-thirds power of the body weight) *multiplied by a factor correcting for age.* In Table 12 are shown the data obtained when the vitamin requirement for the experimental animals, as *calculated* by formula 12, is compared with that observed in the actual tests made in the laboratory. These data of interest are shown in the last two columns of Table 12.

1. Brody's formula is as follows:

$$\frac{W}{A} = 1 - e^{-k\,(t-t*)} \tag{15}$$

where W is the weight of the individual at time t, A is the mature weight, k is the fraction of decline in the time-rate of growth, and $t*$ is the zero time from which t is determined.

On the basis of a comparison of the curative activity of their vitamin B preparation torulin upon adult pigeons and adult white

TABLE 12

Comparison of the Observed Vitamin B Requirement for Different Species with the Requirement as Calculated by the Formula

$$\mathrm{VIT} = 4.9\, W_i^{0.66} \frac{W_i}{W_{max}}$$

SPECIES	W_{max} OF SPECIES	W_i	VIT	
			Observed	Calculated
	grams	*grams*	*mgm.*	*mgm.*
Mouse	34	14*	10	12
		20*	20	21
		23*	30	27
		26*	40	33
Rat	520	97*	20	19
		129*	30	31
		153*	45	41
Pigeon	1,350	300	40	49
		310	60	52
		350	60	63
		390	120	76
		410	80	82
		415	80	84
		420	85	86
		420	90	86
		420	85	86
		420	90	86
		440	95	92
		440	100	92
		450	100	96
		465	100	101
		465	100	101
		485	130	109
		500	120	114
		510	120	118
		520	120	122
Dog	72,000	4,550	90	85
		6,000	165	135
		8,000	232	218
		9,850	360	308
		10,000	360	316
		11,000	384	370

* Average.

rats, Kinnersley, Peters and Reader (1930) are inclined to disagree with our view that the rat requires *relatively* more vitamin B than the pigeon. Examination of such data as they present, how-

ever, supports our position. With regard to the rats used in their tests they state that the maximum weights of the males and females were 250 and 170 grams, respectively, and that during the 21–24 days of subsistence on the B-free diet leading eventually to the appearance of neuromuscular symptoms, these animals decreased in weight and finally weighed from 100 to 120 grams. Applying our formula for the rat to these animals weighing 100–120 grams we find that they need from 22 to 29 milligrams of our standard powder per day. It should be borne in mind that this would be sufficient only to keep these rats free from nervous symptoms of vitamin B deficiency; it would not be the same as the quantity required to allow these rats to maintain their weights at the original levels under conditions which would be normal.

In their paper Kinnersley, Peters and Reader (1930) do not give the weights of the pigeons used in their tests. Inasmuch as they employed a curative technique, and this involves a considerable loss in body weight on the part of the test birds, it is reasonable to assume that these pigeons weighed much less than the 300 grams, which is an average weight of healthy pigeons; it is likely, therefore, that their birds at the time of the curative tests weighed between 200 and 250 grams. Applying our formula to pigeons with these body weights we learn that such birds require from 25 to 34 mgm. of our test powder. This should be compared with the values 22 to 29 mgm., stated above, as the estimated requirements of the rats used.

Our formulae indicate that, relative to body weight, the rat species requires more vitamin B than the pigeon. The values of the respective equating constants for the species formulae support this statement. When these formulae are applied to the *particular rats and pigeons used* in the tests by Kinnersley, Peters and Reader, essentially the same ranges of values for the vitamin requirement are obtained. The curative activity data reported by these investigators, and based upon these particular tests, show a variation that is even greater than that indicated by our calculations for the two species. (See Kinnersley, Peters and Reader, 1930, last column of their Table 1, page 1822.) From this it may be concluded that the disagreement of the data of Kinnersley, Peters and Reader with our results is only apparent and not real.

CHAPTER VIII

ANIMAL EXPERIMENTS: CONFIRMATION OF THE VITAMIN FORMULA BY EXPERIMENTS IN WHICH BODY WEIGHT IS KEPT CONSTANT AND THE METABOLISM FACTOR IS INCREASED

IT IS quite generally agreed that the characteristic symptoms of vitamin B deficiency do not appear as readily in animals subjected to complete starvation as in those who eat appreciable amounts of the ration deficient in this dietary essential. From this point of view the loss of appetite for the B-deficient diet may be regarded as a reaction protecting the animal against development of an unfortunate syndrome. This also suggests that the *total metabolism*, or else the *metabolism of ingested food* is of greater significance here. In discussing the vitamin formula obtained in these animal experiments it has already been pointed out that the expression $W_i^{0.66}$ may be regarded as indicating metabolism, in which case, then, expression 5 (page 56) may be written

$$\text{Vitamin} = \text{K}\cdot\text{Weight}\cdot\text{Metabolism}. \tag{16}$$

From expression 16 it is obvious that

$$\frac{\text{Vitamin}}{\text{Weight}} = \text{K}\cdot\text{Metabolism}, \tag{17}$$

and that in any experiment where the weight is kept constant but the metabolism factor is increased, the vitamin requirement should increase correspondingly. Two ways in which the total metabolism of an animal may be increased are (*a*) by means of forced exercise with consequent ingestion of larger amounts of food and (*b*) administration of thyroid. A study of the effect of exercise and of thyroid administration on the requirement for vitamin B, therefore, should yield data tending either to support or to disprove the interpretation given the quantitative studies already described.

The animal body's capacity for storage of vitamin B is fairly

limited, in contrast to its ability to store other dietary factors, the fat-soluble vitamin A substance, for example. This fact may be utilized in studies of the type here described.

The behavior of dogs restricted to a B-deficient ration has already been discussed. The first symptom indicative of lack of this vitamin is anorexia. We have found that when dogs are given several large daily doses of vitamin B-rich material in order to "saturate the tissue reservoir," so to speak, the time required for this anorexia to appear is quite uniform. In the vast majority of cases about 21 days are required, with some animals exhibiting this anorexia as early as 18 or 19 days, and relatively few dogs showing it after as many as 30 or 33 days. If coprophagy occurs, the animal will not lose its urge to consume the experimental ration unless muzzled. It is reasonable to assume that when, under carefully controlled experimental conditions, a marked shortening of this period occurs, there has been a more rapid exhaustion of the vitamin store probably through consumption in metabolism or loss by excretion, or both. The period required for this anorexia to develop, therefore, may be taken as evidence that the store of vitamin B has been depleted and requires replenishing.

Effect of Exercise on the Time Required for Development of Anorexia Due to Lack of Vitamin B

Five dogs were used in this study. Each animal was its own control with respect to the one variable, namely exercise, studied in these experiments. Each dog was first given a large amount of vitamin B in the form of vitavose[1] in order to bring about a condition of "vitamin saturation." The animal was then allowed to subsist on the vitamin B-deficient ration shown in Table 5 (page 41) and the time required for development of the characteristic anorexia determined. When the urge to eat was lost, control experiments were performed in some cases by administering beef extract by stomach tube with subsequent negative effect on the anorexia; finally the urge to eat was restored by the administration of vitavose, thus proving that the loss of appetite was really the characteristic one due to lack of vitamin B. After a rest period of subsistence on the complete diet, the experiment was repeated but

1. From E. R. Squibb and Sons, New York, N. Y.

with the dog given forced exercise sufficient in degree to insure a daily intake of a significantly larger amount of the food in order to maintain the original body weight.

The exercise was afforded by means of a suitable treadmill operated by an electric motor at a speed kept constant as far as possible. The animals were given a preliminary period of training sufficient to be able to run from 45 to 90 minutes daily without interruption and exhaustion. Over another period of at least a week the animals were exercised and the extra amount of food required to maintain the original body weight under these conditions was determined. During this period the animals received liberal amounts of vitavose.

TABLE 13

The Effect of Exercise on the Time Required for the Development of the Anorexia in Dogs Due to Lack of Vitamin B

DOG	BODY WEIGHT WHEN		FOOD INTAKE DAILY WHEN		DURATION OF DAILY EXERCISE	TIME ON DEFICIENT DIET REQUIRED FOR DEVELOPMENT OF ANOREXIA WHEN		RATIO $\frac{y}{x}$
	Not exercised	Exercised	Not exercised	Exercised		Not exercised x	Exercised y	
	kgm.	*kgm.*	*grams*	*grams*	*minutes*	*days*	*days*	
C	7.8	7.8	118	128	45	21	13	0.61
I	11.4	10.5	135	200	90	21	11	0.52
F	12.0	12.0	183	193	45	18	10	0.55
G	12.0	12.3	180	250	90	18	8	0.44
D	13.7	13.8	150	200	90	24	14	0.58

In each case of increased exercise the period required for the development of anorexia characteristic of lack of vitamin B was decreased by from one-third to one-half the time required when the dogs were not exercised. When the loss of appetite had been corrected by administration of a sufficient amount of vitamin B, the animals maintained their appetite, even though they were still exercising. The data are summarized in Table 13.

In view of the unanimity of the results shown in Table 13, it was felt that further trials with this type of experiment were unnecessary. These findings certainly support the interpretation given the quantitative studies described in the preceding chapters, namely, that the *vitamin requirement per unit of mass is propor-*

tional to the metabolism of that mass. They indicate that the factor $WEIGHT^{0.66}$ in expression 12 (page 61) signifies metabolism, and that some other entity, such as Calories, for example, might perhaps be substituted for it. This idea will be developed later.

Effect of Thyroid Administration on the Anorexia Characteristic of Lack of Vitamin B

Experiments with Dogs

Essentially the same method was used here as that employed in the exercise experiments described above. The minimum amount of the artificial food mixture containing vitamin B that will serve to maintain the animal's body weight under the conditions of cage life, is first determined. The dog is then "saturated with vitamin B" by several large successive daily doses of a good source of vitamin B. The basal diet alone, without the vitamin supplement, is then fed and the number of days required for appearance of the characteristic anorexia is again determined. In the present study hyperthyroidism was induced by daily administration of 5 grams of desiccated thyroid (Armour's) over the periods indicated for the respective dogs in Table 15.

Four dogs were used in this study. In the case of dogs 1 and 2, the observations during hyperthyroidism were made first; with animals 3 and 4, observations during "normal" conditions were made and then the condition of hyperthyroidism studied.

Dogs 1 and 2 had previously maintained their urge to eat a diet of commercial dog biscuit satisfactorily over a period of at least three months. When they were given 5 grams of desiccated thyroid daily, they exhibited a marked loss of appetite for the ration after two weeks, and, as a consequence, lost considerable weight. During the next three weeks occasional administrations of vitamin B were followed in every case by a restoration of the urge to eat, as evidenced by the daily voluntary consumption of larger amounts of food. These preliminary observations were so striking that it was deemed advisable to feed an artificial ration and that described in Table 5 was used. For 18 days the animals were given 10 grams per day of Yeast Vitamine Powder (Harris) as part of the experimental routine, as a result of which they proceeded to

regain their initial weight. The degree of hyperthyroidism induced is indicated by the fact that on the 56th day of thyroid administration the animals were *voluntarily* eating an amount of the artificial ration containing approximately 1200 Calories, an intake about twice that characterizing dogs of similar size but not receiving thyroid (Cowgill, 1928). The administration of vitamin B was then discontinued, and, as a result, anorexia appeared in 20 and 17 days with dogs 1 and 2 respectively. During their respective periods animal 1 consumed an average of 1166 Calories and dog 2 an average of 1231 Calories per day. In both cases, administration

TABLE 14

The Caloric Intake of Dogs in Vitamin B Deficiency as Affected by the Administration of Desiccated Thyroid Tissue

PERIOD OF VOLUNTARY FOOD INTAKE		DOG 1	DOG 2	DOG 3	DOG 4	AVERAGE FOR THE GROUP
Control period, without thyroid	Days in the period..	34	39	23	31	32
	Calories ingested per day.........	600	720	656	635	650
	Total Calories ingested for the period..........	20,400	28,080	15,088	19,685	20,813
Experimental, hyperthyroidism	Days in the period..	20	17	12	20	17
	Calories ingested per day.........	1,166	1,231	1,011	1,213	1,155
	Total Calories ingested for the period..........	23,320	20,927	12,132	24,260	20,160
Average total Calories ingested.		21,860	24,503	13,610	21,872	20,486 (group) 20,461 (individuals)

of the missing vitamin was followed by a return of the urge to eat. The thyroid administration was then discontinued and the animals were allowed a period of six months during which to recover from the effects of the thyroid. The vitamin B requirement was again determined for these dogs using the plan described above. Dog 1 exhibited anorexia after 34 days during which it ate an amount of the ration approximating 600 Calories per day; and dog 2 lost the desire to eat after 39 days during which period it ate an average of 720 Calories per day. The data are shown in Table 14.

In the experiments with dogs 3 and 4 the periods required for

the characteristic anorexia to develop under "normal" conditions were determined first and then the effect of thyroid administration was studied. The data thus obtained are included in Table 14.

It will be noticed in Table 14 that the voluntary caloric intakes of the *individual dogs* until anorexia appeared, as well as the *animals considered as a group* were fairly constant either with or without the administration of thyroid. The data in Table 15 show that the loss of body weight so characteristic of hyperthyroidism is readily corrected by administration of vitamin B. Obviously the loss in weight is due chiefly, if not solely, to an insufficient food

TABLE 15

The Effect of Administration of Vitamin B on the Body Weight in Experimental Hyperthyroidism

	BODY WEIGHT (KGM.)			
	Dog 1	Dog 2	Dog 3	Dog 4
Initial	11.5	12.5	14.4	10.5
After thyroid administration for number of days indicated	10.6 14 days	11.1 14 days	13.2 17 days	9.5 24 days
After 21 days of occasional administrations of vitamin B	9.9	8.5		
After daily administrations of vitamin B for number of days indicated	11.5 18 days	10.6 18 days	13.9 5 days	10.4 9 days

intake, and it appears reasonable to conclude that this is due to loss of the urge to eat as a result of lack of vitamin B.

It appears obvious, that the results of these tests of vitamin B supply in relation to the increased metabolism in hyperthyroidism support the interpretation of the vitamin formula previously expressed, and indicate that the factor WEIGHT$^{0.66}$ in formula 12 signifies metabolism.

There are various reasons why the caloric intake can be regarded only as a first approximation to the true metabolism. Evidence is at hand showing that in hyperthyroidism changes occur in the proportions of the various foodstuffs that are oxidized. Kommerell (1929) observed that the increase in metabolism due to thyroid

administration in starved animals was accounted for by a 31 percent increase in oxidation of protein and 69 percent increase in fat catabolism. Sanger and Hun (1922) also noted an acidosis in hyperthyroidism when the carbohydrate stores were depleted. Determinations carried out on the urines of dog 1 and 2 during the first 32 days of thyroid administration showed that small amounts of acetone were being eliminated daily. The loss of energy represented by the acetone bodies excreted through the lungs and kidneys would be another source of error, if the food intake was taken as a measure of the total metabolism, particularly during hyperthyroidism. In the light of these considerations, therefore, the agreement of the data for voluntarily ingested calories in the two periods, namely, with and without thyroid administration, may be regarded as good. Evidently, then, the tissue stores of vitamin B were drawn upon during the periods when the animals maintained their normal urge to eat, and this supply was consumed in the metabolism of a fairly definite quantity of foodstuffs; the amount oxidized during the period of hyperthyroidism was about the same as that for the control period. This finding emphasizes once more the relation of vitamin B to the metabolism of one or more of the foodstuffs, a conclusion which numerous investigators have reached (Funk, 1914; Randoin and Simonnet, 1923; Evans and Lepkovsky, 1929).

This increase in the vitamin B requirement associated with a rise in the metabolic rate may explain some of the observations reported in the literature. In her study of hyperthyroidism in dogs, Kunde (1927) noticed that some of her animals lost considerable weight in contrast to other dogs in which maintenance of weight occurred. In view of the data shown in Tables 14 and 15, it appears reasonable to assume that vitamin B deficiency was a complicating factor in Kunde's experiments, and that the animals which lost weight needed more of this dietary factor, presumably to maintain the urge to eat. Steenbock, Sell and Nelson (1923) and others have shown that when rats have access to their intestinal excreta, they require a smaller amount of vitamin B in the food than is the case when coprophagy is prevented. We have made similar observations on dogs. It is possible that those of Kunde's animals that maintained their weights, were coprophagists. Abelin,

Knuchel and Spichtin (1930) observed that depletion of glycogen stores of liver and muscle in hyperthyroidism is prevented when the animals are fed diets rich in vitamins; no data were published by these investigators concerning the amounts of food consumed in their experiments, but it is significant that the animals which subsisted on the rations containing large amounts of vitamins showed a weight loss only half as great as those fed on diets low in vitamin content. Such a result might be expected in view of the findings reported in Tables 14 and 15.

Experiments with Pigeons

Inasmuch as pigeons are widely used for vitamin B studies, and the study in dogs of the vitamin B requirement in relation to hyperthyroidism yielded such striking results, it appeared advisable to determine whether similar results would be obtained with the pigeon. The plan of investigation consisted first of all in determining the least amount of a given vitamin concentrate required to maintain the individual bird's body weight at as constant a level as possible over a period of days under normal conditions; then, the maintenance dose of the same vitamin preparation was determined after the group of pigeons had received daily administrations of minimal amounts of desiccated thyroid sufficient to produce a moderate to severe degree of hyperthyroidism.

The results of such a study are shown in Table 16, where it will be seen, that in a state of hyperthyroidism there is an increase in the amount of vitamin B required to maintain the normal urge to eat.

In these experiments there was not the same degree of correlation in different birds between the increased amount of vitamin B required in hyperthyroidism over that needed under normal conditions. For example, bird VI required 100 mgm. of vitamin concentrate to maintain its body weight at 373 grams under normal conditions whereas 500 mgm. were required to maintain this pigeon's weight at 335 grams when it was receiving desiccated thyroid. This should be compared with the data for bird X which show that a maintenance weight of 340 grams under normal conditions was associated with a vitamin dosage equal to that of bird VI, and this vitamin requirement was raised to only 200 mgm.

by feeding thyroid. Because no determinations of basal metabolic rate were made in these experiments, it is impossible to say that these differences are to be attributed simply to variations in the effects of the ingested thyroid. It is possible that different birds are characterized by differences in gastro-enteric function, particularly in relation to utilization of ingested vitamin B, in which case variations of the type shown in Table 16 might be expected.

The experiments described in this chapter constitute ample confirmation of the interpretation placed on the numerous quantitative experiments described in the preceding chapters, that *the vitamin requirement of an organism per unit of mass is proportional to the metabolism of that mass.*

TABLE 16

The Vitamin B Requirement of Pigeons under "Normal" Conditions and during Experimentally-Induced Hyperthyroidism

BIRD	"NORMAL" CONDITIONS		HYPERTHYROIDISM	
	Body weight average	Maintenance dose of vitamin B concentrate	Maintenance dose of vitamin B concentrate	Body weight average
	grams	*mgm.*	*mgm.*	*grams*
D	302	70	100	274
IV	297	80	100	273
II	293	80	Died	
IX	277	80	Died	
A	276	80	Died	
VII	286	90	Died	
III	275	90	150	256
I	314	90	300	240
V	343	100	150	290
X	340	100	200	338
VI	373	100	500	335
VIII	347	100	Died	

Is the Metabolism Factor Which is Related to the Vitamin B Requirement to be Regarded as Total Calories or the Amount of Some Particular Foodstuff?

It is of interest to inquire whether the data obtained in these investigations throw any light upon the question as to the relation of vitamin B to the metabolism of particular foodstuffs. Funk (1914), Braddon and Cooper (1914), Randoin and Simonnet (1923)

and others have expressed the view that this vitamin is in some way related to the metabolism of carbohydrate. In Funk's experiments, actually very little difference was obtained when he substituted protein for much carbohydrate in diets fed to pigeons, and observed the time required for the birds to develop symptoms of extreme vitamin B deficiency. Braddon and Cooper (1914) suggested that the caloric value of the diet was the factor of importance, and mentioned carbohydrate secondarily, evidently in an attempt to explain why a diet preponderantly of polished rice should be so effective in producing the extreme condition of B-deficiency. The findings of Hartwell (1928) have been cited as favoring the view that protein metabolism involves vitamin B, but her experiments have not been confirmed (Sherman and Gloy, 1927; Francis, Smith and Moise, 1931). On the other hand, Green (1918) and Plimmer (1926), Plimmer, Rosedale and Raymond (1927) contend that vitamin B function is related to Calories metabolized irrespective of type of foodstuff: that the *total caloric intake* rather than that of any particular foodstuff (carbohydrate, protein or fat) is the common denominator of interest. According to Evans and Lepkovsky (1929) less vitamin B is required when there is a large amount of fat in the diet; in other words, fat acts to spare vitamin B. The most striking results in this connection are obtained when lard is used. Unpublished experiments of our own may be interpreted as confirming Evans and Lepkovsky. (For further discussion of this topic see page 97.)

In Table 17 are shown the Calories contributed to the various experimental diets used in these animal experiments by protein, fat and carbohydrate (*a*) in the ration as prepared and offered to the animals, and (*b*) as metabolized, assuming that 58 percent of the protein is converted to carbohydrate and then metabolized.

It will be noticed in Table 17 that in the case of the pigeons the amount of fat ingested was almost negligible, being only 1 percent; the rats ate 28 percent of their calories in the form of fat, and dogs 31 percent. The carbohydrate calories ranged from 26 percent in the case of the dogs to 87 percent for the pigeons. It is an interesting fact that in spite of these wide differences in diets used, essentially the same relation of vitamin need to the $\frac{5}{3}$ power of the body weight was found to exist in the several species. The

data obtained in these studies, therefore, do not indicate any particular foodstuff as related in metabolism to vitamin B. It should be pointed out, however, that the plan of experimentation followed here was not selected for a crucial study of this particular question. Other lines of investigation are undoubtedly necessary in order to determine whether vitamin B function is related to the metabolism of carbohydrate or the other foodstuffs yielding energy. From the point of view of a practical application of these findings in human nutrition, our own experiments indicate the total caloric intake as the factor to which to relate the requirement for vitamin B.

TABLE 17

The Distribution of Calories among the Proximate Principles of the Various Diets Used in These Feeding Experiments with Different Species

DISTRIBUTION OF CALORIES AMONG PROXIMATE PRINCIPLES OF THE VARIOUS DIETS	SPECIES			
	Mouse: diet 5 C. per gram	Rat: diet 5.2 C. per gram	Pigeon: diet 4 C. per gram	Dog: diet 4.7 C. per gram
	percent	*percent*	*percent*	*percent*
Fraction of total calories from:				
Protein	25	19	12	43
Fat	44	28	1	31
Carbohydrate	31	53	87	26
Fraction of total calories assuming that 58 percent of the protein is metabolized as carbohydrate:				
Protein	10	8	5	18
Fat	44	28	1	31
Carbohydrate	46	64	94	51

Hendricks (1933) has recently confirmed this in studies of the maintenance requirements of growing chicks. He has offered a differential equation for describing the relation between the live weight and feed consumption of a growing animal. Following the suggestion made in one of our papers, pointing to the $\frac{5}{3}$ power of the body weight as a factor of importance, Hendricks has found that it is likewise significant in his equation by which the total metabolism of the animal is expressed. Hendricks states the matter thus:

The metabolism, at least in the case of the chicken, appears to be proportional to the 5/3 power of the live weight. . . . Since recently published work by Cowgill

(1932) shows that the vitamin B requirement of an animal is proportional to the 5/3 power of the live weight, it is probable that the vitamin B requirement is proportional to the metabolism.

The experiments concerning the influence of exercise and hyperthyroidism on the vitamin requirement indicate very clearly that the need for this dietary essential per unit of mass is proportional to the metabolism of that mass. Inasmuch as individuals may readily vary their caloric intake considerably without at the same time undergoing appreciable changes in body weight, it is of considerable practical importance to substitute in expression 12

$$\text{(12)} \qquad \text{VIT} = 4.9\ W_i^{0.66}\ \frac{W_i}{W_{max}}$$

some expression for the factor $W_i^{0.66}$, which we have shown to signify metabolism. Examination of the food intake data obtained, and consideration of what is known concerning the basal metabolic levels of the species here studied, lead to the conclusion that formula 12 applies to individuals whose total daily caloric exchange is represented by the expression

$$\text{(18)} \qquad \text{CALORIES}_{\text{per day}} = 1.5\ \text{WEIGHT}_{\text{grams}}^{0.66}$$

In other words, their total energy level was about 50 percent above the basal metabolic level. From 18 it is evident that we have an expression for Calories which can be substituted for $W_i^{0.66}$ in expression 12. One then obtains:

$$\text{(19)} \qquad \text{VIT}_i = 4.9\ \frac{\text{Calories}}{1.5} \cdot \frac{W_i}{W_{max}}$$

whence,

$$\text{(20)} \qquad \frac{\text{VIT}_i}{W_i} = \frac{3.27}{W_{max}} \cdot \text{CAL}$$

or,

since the maximum weight of the species here is a constant,

$$\text{(21)} \qquad \frac{\text{VIT}_i}{W_i} = \text{K}_s \cdot \text{CAL}_i,$$

where VIT_i signifies the vitamin required daily by a given individual whose body weight is W_i, and whose daily total energy exchange

is CAL_i; K_s is the species constant, the precise value of which depends upon the maximum normal weight of the species, and the vitamin potency of the preparation in terms of which the daily requirement is being stated.

In view of the fact that animals and man normally govern their food intake according to their energy need, the value of any ration in supplying sufficient amount of vitamin B to a given individual will depend upon the value of the ratio of the vitamin content to the energy content. This being true, a more practical expression for evaluating diets with respect to vitamin B than 21 above would be

$$\frac{VIT_i}{CAL_i} = K_s \cdot W_i \cdot \tag{22}$$

A Vitamin B Formula Applicable to Man

In order to apply such a formula as 22 to the human species it is necessary first of all to determine the proper value for the maximum normal weight of man. To do this the tables of Medico Actuarial Investigations of the Association of Life Insurance Medical Directors (1912, Vol. I) were examined. Here we find[1] that the graded average weight for men 6 feet, 5 inches in height, age 50 to 54 years, is 218 pounds, or approximately 100 kgm. In another table,[2] however, are given data for slightly taller men, ranging from 6 feet 6 inches to 6 feet 9 inches, with weights of 245, 260 and 263 pounds respectively. The average weight of this group proves to be 256 pounds, or approximately 115 kgm.[3] This figure has therefore been taken as the maximum normal weight for the human species to be used in a formula of type 22. The formula for the human species becomes:

$$\frac{VIT_i}{CAL_i} = \frac{3.27}{115{,}000} \cdot W_i \tag{23}$$

or

1. Ass. Life Ins. Med. Dir., Vol. I, Table III.
2. Ass. Life Ins. Med. Dir., Vol. I, Table I.
3. It should be remembered that the men represented by this average weight were unusually large but were nevertheless considered sufficiently normal to be insurable.

$$\frac{\text{VIT}_i}{\text{CAL}_i} = 0.0000284 \text{ WEIGHT}_{\text{grams}} \cdot \tag{24}$$

In chapters XI–XIII, inclusive, we shall show, by a study of various human diets, that this formula predicts with a fair degree of accuracy the requirement of human beings for vitamin B.

CHAPTER IX

THE AMOUNT OF VITAMIN B PRESENT IN DIFFERENT FOODS

The Need For a Common Vitamin B Unit

BEFORE diets can be properly evaluated with respect to vitamin B it must be possible to express the amounts of the vitamin present in different foods in terms of a common unit. Different investigators have made attempts to supply such a unit, but up to the present time no single suggestion in this respect has met with general use.

Sherman and his associates have chosen as their unit the vitamin required to permit a young rat weighing from 40 to 50 grams to gain about 3 grams per week over a period of 8 weeks. Roscoe (1930) feeds the experimental diet to young rats weighing about 40 grams, and observes the growth of the animals over a period of 5 weeks; the amount of increase in body weight over this period permitted by the ration is taken as a measure of the amount of vitamin B furnished by the supplement being tested. The foods are compared on the basis of the amounts of each required to permit an increase in body weight of from 50 to 60 grams in 5 weeks.

Other investigators have worked with the pigeon or domestic fowl. Plimmer, Raymond and Lowndes (1929, 1931, 1933) assayed many common foods by such a technique. Jansen and Donath (1927) have used native rice birds—bondols—in their assays performed in Java.

In 1931 an international committee, working under the auspices of the League of Nations Health Organization considered the matter of establishing suitable international standards for the vitamins. As the unit for vitamin B this committee finally selected the biological activity—effect on test animals—of 10 mgm. of a fuller's earth adsorbate of vitamin B prepared from an extract of rice polishings according to the technique elaborated by Seidell

(1916) and Jansen and Donath (1927). Test samples of this adsorbate have been prepared for distribution to various laboratories engaged in vitamin research, thus making it possible for different groups of investigators to express their results in terms of a common unit.

The assay reported in Table 1 (see page 24) was made on such material.

The Milligram-Equivalent: A Unit Based on the Present Studies

The studies of the vitamin B requirements of different species reviewed in the preceding chapters were made with the same vitamin concentrate. It is obvious that the data thus obtained make it possible to deal effectively with any assay data in the literature obtained from either the rat or the pigeon and to express the results of such food assays in terms of the same product, namely lot 985 of the yeast concentrate used in these investigations. The literature dealing with the assay of foods for vitamin B has therefore been surveyed and the results of various tests expressed in terms of the *milligram-equivalent* of our tested standard powder. By milligram equivalent is meant the *number of milligrams of our tested powder equivalent in vitamin B content to one gram of the food.* In the case of liquid foods, milk, for example, one cubic centimeter, rather than one gram of the food is the unit quantity used in the comparison.

How to Estimate the Milligram-Equivalent Index Value of a Food From Pigeon Data

Where data obtained with the pigeon are being considered, two procedures have been used. If the data show the actual body weights of the pigeons, then the requirements of birds of those weights in terms of our standard powder are determined by reference to our data contained in Table 12 (page 63). For example, suppose the bird weighed about 300 grams. Reference to Table 12 shows that such a bird requires about 50 mgm. of our test powder per day. Let us assume that this bird received 250 mgm. of a dried yeast daily as a supplement to a B-deficient diet, and, as a

result, maintained its body weight for a considerable period. The vitamin B index for this particular yeast then calculates to be:

$$50 \text{ mgm. standard powder} \div 0.25 = 200 \text{ mgm. equivalents}$$

In certain studies, such body weight data are not given, but numerous foods are listed as having values relative to each other. Among the foods in the list appear some for which quite accurate assays are already available as a result of work done in our own laboratory. For example, Plimmer, Raymond and Lowndes (1933) published such a list of foods and in this appears wheat germ ("Bemax"). By assigning to this product the value indicated by our own assay, we can then give the other foods relative values shown by their positions in the list as given by Plimmer and associates. It is an interesting fact that many foods have been assayed by both the pigeon and the rat technique by different groups of investigators, and the results of our calculations agree remarkably well as to the number of milligram-equivalents to be assigned to these foods. For illustrations of this the reader should examine Table 21 particularly with reference to barley, wheat bran, wheat germ, whole wheat, and lentils.

How to Estimate the Milligram-Equivalent Index Value of a Food From Rat Data

When the assay data were obtained from rat experiments, it was necessary to ascertain, by study of either the growth curves or the tables given in the paper, the average body weights reached by the experimental animals, and then to determine from our own data the daily vitamin requirement of rats of this body weight in terms of our test powder. For example, Burton (1928) found that when young rats received 0.8 gram daily of raw turnip greens, they went from 48 grams to about 56 grams in 8 weeks. According to our own work, a rat weighing 56 grams requires from 8 to 10 mgm. daily of our test powder. Therefore:

$$8 \text{ or } 10 \text{ mgm.} \div 0.8 = 10 \text{ or } 12 \text{ mgm. equivalents}$$

Many foods have such a small amount of vitamin B that they can be assayed only by incorporating them in the diet in relatively large amounts. In such cases, it is necessary not only to ascertain

the body weight which the animals attain on the test ration, but to determine the approximate amount of the food in question which is eaten daily by animals of this weight. This may be done by utilizing the energy intake data collected by Osborne and Mendel (1915) and shown in Table 18. The daily energy exchange in Calories for a rat of the size indicated by the assay data is estimated from this table. Upon dividing this number of Calories by the energy value of the test ration per gram, one secures the approximate daily intake of the food in grams. From this and

TABLE 18

The Daily Calorie Intake of the White Rat

The data presented in this table are the results of calculations based on the food intake data collected by Osborne and Mendel, Journal of Biological Chemistry, vol. 22, pp. 241–258, 1915, particularly Table A, page 244. The energy value of the food used was approximately 5 Calories per gram.

BODY WEIGHT		AVERAGE FOOD INTAKE PER WEEK		CALORIES PER DAY	
Range	Average	Males	Females	Males	Females
grams	*grams*	*grams*	*grams*		
30–50	40	25	25	17.9	17.9
50–75	63	29	30	20.7	21.4
75–100	88	38	38	27.1	27.1
100–125	113	38	42	27.1	30.0
125–150	138	47	48	33.6	34.3
150–175	163	55	55	39.3	39.3
175–200	188	61	61	43.6	43.6
200–250	225	64	66	45.7	47.1
250–300	275	75		53.6	
300–350	325	87		62.1	
350–390	370	90		64.3	

knowledge of the composition of the ration one can readily estimate the probable daily intake of the food in question. The number of milligrams of test powder required by animals of the size under consideration is estimated from the formula for the rat species (page 54); this, divided by the daily intake of the food in question gives the vitamin index for this food.

How to Correct For Error Due to Coprophagy

WHENEVER considering data obtained from rat experiments one must determine whether coprophagy on the part of the experi-

mental animals was allowed or prevented. All food assays on rats made prior to about 1923 involve the coprophagy error. Subsequent to the appearance of the paper by Steenbock, Sell and Nel-

TABLE 19

The Influence of Coprophagy on the Tests to Determine the Vitamin B Minimum in the Rat

RAT	TEST SUBSTANCE GIVEN AS SOURCE OF VITAMIN	BODY WEIGHT ATTAINED WHEN GROWTH RATE BEGAN TO DIMINISH SIGNIFICANTLY			
		"Old Style" cage that permits coprophagy		"New Style" cage with raised screen bottoms to prevent coprophagy	
		Daily test dose	Body weight reached	Daily test dose	Body weight reached
		mgm.	*grams*	*mgm.*	*grams*
902	"Wheat sugar"	200	170		
903	"Wheat sugar"	200	164		
901	"Wheat sugar"	200	120		
900	"Wheat sugar"	200	173		
Average		200	156		
899	"Wheat sugar"			200	92
898	"Wheat sugar"			200	105
897	"Wheat sugar"			200	94
896	"Wheat sugar"			200	80
Average				200	93
899	"Wheat sugar"			300	102
898	"Wheat sugar"			300	172
897	"Wheat sugar"			300	153
896	"Wheat sugar"			300	110
Average				300	134
415	Yeast concentrate	30	248		
413	Yeast concentrate	30	190		
410	Yeast concentrate	30	190		
Average		30	209		
Data in Table 9	Yeast concentrate Average Average			 20 30	 97 129

son in 1923, most investigators have controlled against this source of error. We have performed some experiments in an endeavor to evaluate this error. Two different sources of vitamin B, one pre-

pared from wheat germ, called "wheat sugar," and the other from yeast, were assayed twice on young rats, the first time with the animals housed in the old-style cage which permitted coprophagy, and the second time with the rats confined in cages with wide-mesh raised bottoms which allowed the feces to fall beyond the reach of the animals.

In Table 19 are given the essential data obtained from these tests. It will be noticed that whereas 200 mgm. per day of the "wheat sugar" permitted the animals to go to an average of 156 grams body weight when in the old-style cages, the same dose of this material given to animals housed in the new-style cage permitted growth to a weight of only 93 grams. Similarly, in the case

TABLE 20

The Effect of Coprophagy upon the Value of the Vitamin Index Yielded by Assays with the Rat

	"WHEAT SUGAR"		YEAST CONCENTRATE	
	Old cage: coprophagy permitted	New cage: coprophagy prevented	Old cage: coprophagy permitted	New cage: coprophagy prevented
Test dose given daily, mgm.	200	200	30	30
Average body weight attained by animals, grams	156	93	209	129
Vitamin index value yielded by these data	205	101	227	100
Index *with old cage* / Index *with new cage*	2.03		2.27	

of the yeast concentrate, 30 mgm. per day for animals having access to their feces gave growth to an average weight of 209 grams, whereas this amount fed to rats in the new-style cage resulted in an average body weight of only 129 grams.

One may calculate the vitamin index values yielded by the data representating the two conditions of cage life. The results of such calculations are presented in Table 20. Comparison of the vitamin index values (see last row of Table 20) indicates that the vitamin B requirement measured under conditions where coprophagy is prevented is approximately twice as great as that determined when the animals have access to their feces.

In view of the results presented in Tables 19 and 20, it appears

reasonable to introduce, when necessary, a correction for the coprophagy factor. This has been done simply by multiplying the amount of food eaten in the test by two and using the resultant quantity as the amount of the food to be regarded as equivalent to the number of milligrams of test powder required by the test animals.

Vitamin B Index Values of Foods

Using the methods just described, vitamin index values have been estimated for as many foods as possible. The results of these calculations are presented in Table 21. In constructing this table an attempt has been made to show not only the index value but the source of data used, the kind of biological test involved in the assay, and, where many tests have been made on the same food, the index value finally selected for that food. In some cases the value chosen represents an average of different results. In other instances, the choice has been based upon various considerations. The fact that certain tests were made more recently and coprophagy prevented, thus obviating the necessity of introducing a correction for this gives these tests greater weight. In certain experiments it was obvious that the test animals were still growing when the assay was terminated, in which case calculation could only yield a "not less than" value. Furthermore, choice of the index value was always made with the view to its practical application in evaluating human diets. With a food like spinach, for example, which gives an appreciably high index when tested in the raw state, it will be noticed that a much lower value is chosen; this was done because numerous assays of the cooked product—the spinach as eaten by man—indicate a great loss of the vitamin as a result of the cooking or canning process.

Table 21 may seem too detailed to be of practical use. It is made so purposely, in order that the reader may see what data are available with respect to the various foods, and formulate his own judgment as to the validity of the index value finally selected. It is quite likely that some of the values are only very roughly approximate, and future research will indicate that they ought to be changed considerably. Some investigators may feel that most of the assays made previous to about 1929 merit little if any consider-

ation because vitamin G (B_2) may have been a limiting factor in retarding the growth of the animals used in the assay, and therefore, that calculations of an index value from the data yielded by such assay are of no value. In answer to this objection it may be pointed out that in such a case the true value of the index must be greater than that indicated in Table 21 for this food. Even in the face of these admitted shortcomings of the data presented in Table 21, the critic will probably admit that they constitute a slight step forward toward a solution of the problem of evaluating a human diet with respect to vitamin B. If we are able to show that use of these index values with various diets gives results agreeing very well with the facts known concerning the incidence of beriberi among the persons who subsisted on the respective diets, then it will probably be admitted further, that the data in Table 21 are of definite practical value, and that man's requirement for vitamin B has been ascertained to an unexpected and moderately accurate degree. In succeeding chapters we present for consideration the vitamin B contents of various human diets as ascertained by means of the index values of foods presented in Table 21.

Discussion of Data in Table 21

Examination of Table 21 reveals numerous points of interest. The common cereals in the whole-grain form have very nearly the same index, the average value being about 20. It is a curious fact that the whole-grain cereals have about the same vitamin B content per gram as the solids of cow's milk and of hen's egg. This average value is slightly less than that for most of the members of the legume group. The red kidney bean and the peanut have much higher values than dried peas, lentils, haricot beans and soybean, which as a group have a rating of about 23. These relationships agree very well with those reported by Plimmer, Raymond and Lowndes (1931) but do not conform with the statement of Rosedale (1931) who quotes the earlier work of Plimmer and associates which was performed on chickens. It is possible that the results of the earlier work were not due entirely to the vitamin B factor; the periods over which the experiments were carried out were so long that other deficiencies may have been able to develop and thus affect the results. In all probability the index value given for rice

TABLE 21

Vitamin B (B_1) Index Values of Foods

(1) The numerous footnotes—see second column—are listed at the end of the table. References cited here are given in detail in the Bibliography, page 233 *et seq.*

(2) The meanings of the symbols used in the third column are as follows:

Symbol	*Meaning*
gr.	Growth.
mn.	Maintenance.
prev.	Preventive.
calc.	Calculated on basis of assumptions stated in footnote.
n. l. t.	Not Less Than.
n. g. t.	Not Greater Than.
av.	Average.
t. a.	Taken as.

FOOD	FOOTNOTE	BIOLOGICAL TEST AND OTHER SIGNIFICANT COMMENT	INDEX VALUE IN MGM.-EQ. PER GRAM: Yielded by these data	Chosen for this food	CALORIE INDEX: CAL./GM.
			mgm.-eq.	*mgm.-eq.*	
Grains and Grain Products:					
Adlay	1	Rat gr.	5.5	5.5	3.58
Atta, crude	2	Rat gr.	23	23	3.72
Barley:					
"	3	Pigeon mn.	20		
"	4	Rat gr.	21		
" "husked"	5	Pigeon prev.	20	20	3.50
" "kernel"	6	Rat gr., n. l. t.	16	20	3.50
" "pearled"	7	Rat gr., n. l. t.	2	3	3.55
" "unhusked"	5	Pigeon prev.	24		
Buckwheat	3	Pigeon mn.	40	40	3.48
Cambu	7	Rat gr.	16	16	3.68
Cholam	7	Rat gr.	15	15	3.59
Corn:					
" whole kernel	8	Rat gr.	20	20	1.01
" " "	9	Chicken prev.	20	20	1.01
" meal, "old process, low grade"	10	Calc.		20	3.56
Corn meal, "old process, better grade"	11	Calc.		15	3.56
Corn meal, "new process"	12	Calc.		5	3.56
" , sweet, canned comm'l	13	Calc.		10	0.98
Dari	3	Pigeon mn.	20	20	3.50
Indian flour, pure unbleached	2	Rat gr.	23	23	3.50
Macaroni	25	Taken as		3	3.58
Millet	3	Pigeon mn.	26	26	3.45
Oatmeal	3	Pigeon mn.	22	22	3.99
Rice:					
" brown	3	Pigeon mn.	20	20	3.50
" "dead"	1	Rat gr., n. g. t.	3	3	3.43
" glutinous	1	Rat gr.	5.5	5.5	3.47
" polished	14	Rat gr.	1.6	1.6	3.51
" polishings	15	Rat gr.	84	84	4.23
" paddy	7	Rat gr.	13		
" , whole, parboiled	95	Rat gr., t. a.	15	15	3.50
Rye	3	Pigeon mn.	20	20	3.50
Wheat:					
" bran	3	Pigeon mn.	40		
" "	16	Rat gr.	40	40	3.59
" "	17	Rat gr.	39		
" flour	17	Rat gr.	3	3	3.53
" germ	18	Rat gr.	130		
" "	17	Rat mn.	150		

TABLE 21—*Continued*

FOOD	FOOTNOTE	BIOLOGICAL TEST AND OTHER SIGNIFICANT COMMENT	INDEX VALUE IN MGM.-EQ. PER GRAM: Yielded by these data	INDEX VALUE IN MGM.-EQ. PER GRAM: Chosen for this food	CALORIE INDEX: CAL./GM.
			mgm.-eq.	*mgm.-eq.*	
Grains and Grain Products— Concluded:					
Wheat—*Concluded:*					
“ germ	3	Pigeon mn	124		
“ “	53	Pigeon mn	136		
“ “	av.	Taken as		135	3.75
“ middlings	3	Pigeon mn	80		
“ “	20	Taken as	67	75	3.84
“ whole	3	Pigeon mn	20		
“ “	17	Rat gr	20–23		
“ “	7	Rat gr	20		
“ “	21	Rat gr	15		
“ “	..	Taken as		20	3.60
“ bread, white, water	22	Rat gr	2.1		
“ “ “ “	86	Rat gr	1.7		
“ “ “ “	24	Rat gr	1.8		
“ “ “ “	86	Rat gr., av	1.4		
“ “ “ “	..	Taken as		2	2.59
Pulses:					
Bean, coffee, green	27	Pigeon mn., less than	13		
“ “ , roasted	27	Pigeon mn	0	0	
Bean, frijoles (New Mexico)	31	Taken as		20	3.72
“ , haricot	27	Pigeon mn	20	20	2.70
“ , red kidney	26	Rat gr	35	35	1.04
“ , lima	31	Taken as		20	1.23
“ , navy, baked	30	Taken as		10	1.29
“ , soy	27	Pigeon mn	26		
“ , “	28	Rat gr	20–23	23	4.33
“ , in human diets, kind not stated		Taken as		20	3.60
Cicer arientinum (yellow)	2	Rat gr	19	20	3.60
“ “ (red)	2	Rat gr	24	20	3.60
Dhal		Taken as		23	3.50
Lentils	27	Pigeon mn	26		
“ (*Phaseolus mungo*)	2	Rat growth	26	26	3.49
“ (*Phaseolus radiatus*)	2	Rat growth	23	23	3.49
Peanut	27	Pigeon mn	40	40	5.48
Peas, split	27	Pigeon mn	26		
“ , whole dried green	27	Pigeon mn	26	26	3.55
“ , raw, ungraded	29	Rat gr	10–21	15	1.00
“ , normally canned, No. 6	29	Rat gr	7–10		
“ , “ “ , “ 3	29	Rat gr	7–10		
“ , “ “ , “ 1	29	Rat gr	7–10		
“ , canned, in human diets		Taken as		8	0.55
Nuts:					
Almonds, ground	27	Pigeon mn	20	20	6.47
“ , whole	27	Pigeon mn	20	20	6.47
Chestnuts, dried	27	Pigeon mn	20		
“	32	Rat gr	22–25	20	4.03
Cocoanut	27	Pigeon mn	0		
“ , ripe	82	Rat gr. av	4	4	5.90
“ , water	82	Rat gr	0.5–0.7	0	0.34
Filbert, husked	33	Pigeon prev	40	40	7.02
Hazelnut	27	Pigeon mn	40	40	7.10
Nuts, in human diets, kind not stated		Taken as	20	20	6.50

TABLE 21—*Continued*

FOOD	FOOTNOTE	BIOLOGICAL TEST AND OTHER SIGNFICANT COMMENT	INDEX VALUE IN MGM.-EQ. PER GRAM: Yielded by these data	INDEX VALUE IN MGM.-EQ. PER GRAM: Chosen for this food	CALORIE INDEX: CAL./GM.
			mgm.-eq.	*mgm.-eq.*	
Nuts—Concluded:					
Pecan	32	Rat gr., n. l. t.	29		
"	33	Rat gr.	23		
"	33	Pigeon mn.	17–19	20	7.34
Walnut, black	32	Rat gr.	12–13	12	6.64
Vegetables: Roots:					
Artichoke	34	Pigeon mn.	10		
"	35	Rat gr., t. a.	10	10	0.79
Asparagus	36	Rat gr., n. l. t.	14	14	0.29
Beet	37	Taken as		2.4	0.46
Carrot, raw	18	Rat gr.	4.9		
" , "	38	Rat gr.	3.0		
" , "	39	Rat mn.	3.3		
" , "		Taken as		3.7	0.45
" , boiled	39	Rat mn.	2.5		
" , "	40	Taken as		2.8	0.45
Leeks	34	Pigeon mn.	10	10	0.33
Onions	18	Rat gr. av.	2.7	2.7	0.49
" in Japanese diets	88	Taken same as leek		10	0.33
Parsnips	34	Pigeon mn.	14	14	0.65
Poi (Hawaiian food, from taro)	45	Rat gr.	6	6	0.93
Potato, raw white	18	Rat gr.	4		
" , cooked	41	Rat gr.	3.5–4.0		
" , boiled without skin	39	Rat mn.	2.4–4.6		
" , in human diets	42	Taken as cooked		3.8	0.97
Radish	43	Rat gr.	6.2	6.2	0.29
" , pickled Japanese, "takuwan"	87	Taken as		30	0.30
Rutabagas	37	Taken as		2.4	0.41
Sprouts, mung bean, raw	23	Rat gr.	4	4	0.29
" " " , cooked	23	Rat gr.	3.6	3.6	0.29
Sweet potato	44	Taken as		3.0	1.23
Taro	45	Rat gr.	6–8	7	0.77
Turnip	46	Rat gr.	2.4	2.4	0.39
Vegetables: leaves, stalks and fruits:					
Cabbage	28	Rat gr.	4.0		
" , etiolated leaves	46	Rat gr.	4.0	4.0	0.32
" , dark green leaves	46	Rat gr.	3.5		
" , Chinese, fresh	47	Rat gr.	4.5	4.5	0.07
" , " , salted	47	Rat gr.	5.3	5.3	0.07
" , " , bran-salted	47	Rat gr.	25	25	0.45
Cauliflower	48	Taken as		2.4	0.31
Celery	36	Rat gr., n. l. t.	1.0		
"	48	Taken as		2.4	0.19
Collards, raw	49	Rat gr.	11	11	0.49
" , cooked	49	Rat gr.	5.5	5.5	0.49
Cucumbers, raw	50	Taken as		3.4	0.17
" pickles	50	Taken as		1.7	0.16
Eggplant	48	Taken as		2.4	0.28
Greens, raw turnip	49	Rat gr.	11	11	0.29
" , cooked turnip	49	Rat growth	11	11	0.29
" in human dietary, kind not stated		Taken as		10	0.29
Kale		Taken as cabbage		4	0.51

TABLE 21—*Continued*

FOOD	FOOTNOTE	BIOLOGICAL TEST AND OTHER SIGNIFICANT COMMENT	INDEX VALUE IN MGM.-EQ. PER GRAM: Yielded by these data	INDEX VALUE IN MGM.-EQ. PER GRAM: Chosen for this food	CALORIE INDEX: CAL./GM.
			mgm.-eq.	*mgm.-eq.*	
Vegetables: leaves, stalks and fruits—Concluded:					
Kohlrabi, garden	38	Rat gr.	2.5	2.3	0.31
" , greenhouse	38	Rat gr.	2.0		
Lettuce, garden	38	Rat gr.	5.0		
" , greenhouse	38	Rat gr.	4.0	4.2	0.19
"	46	Rat gr.	3.5		
Limu (fresh water algae):					
Limu eleele	45	Rat gr. (about)	2	2	0.12
" lipoa	45	Rat gr. (about)	1.3	1.3	0.07
Peppers, green	85	Taken as		2.2	0.26
Pumpkin, raw	35	Rat gr.	3.4	3.4	0.26
" , canned		Taken as ½ raw		1.7	0.33
Rhubarb	48	Taken as		2.4	0.23
Spinach, raw	51	Rat gr.	11		
" , cooked 7 minutes	51	Rat gr.	5		
" , " 15 "	51	Rat gr.	4		
" , commercial canned	51	Rat gr.	1.7–2.0		
" , home canned	51	Rat gr.	1.7		
Spinach, raw dried	46	Rat gr.	3.2		
" , " "	28	Rat gr.	2.4		
" , " "	52	Rat gr.	1.1		
" , " "	52	Pigeon mn.	1.1		
" , in human dietaries		Taken as cooked		2.4	0.24
" , New Zealand: fresh	54	Rat gr.	6.0	6.0	0.24
Squash		Same as pumpkin		3.4	0.46
Stringbeans, raw, fresh	51	Rat gr.	3.0–3.5	3.1	0.42
" , " "	79	Rat gr.	2.9–3.1		
" : open-kettle cooked	51	Rat gr.	2.3–2.7		
" : commercial canned	51	Rat gr.	1.9		0.21
" : home canned	51	Rat gr.	1.9		
" : in human dietaries		Cooked; some loss		2.2	0.35
Taro leaves	82	Rat gr.	4	4	0.20
Tomato, pulp	18	Rat gr.	2.2		
" , "	28	Rat gr.	2.9	2.6	0.23
" , "	34	Pigeon mn.	2.5		
" , juice, commercial	53	Pigeon mn.	2.8	2.8	0.17
" , dried	18	Rat gr.		36	3.87
Watercress	34	Pigeon mn.	4.0	5.5	0.22
"	46	Rat gr.	7.1		
Fruits:					
Apple	18	Rat gr.	2.2	2.2	0.63
"	55	Rat gr., n. l. t.	1.3		
" , dried		Taken as		6.7	2.91
Apricot, fresh		Taken as apple		2.2	0.58
" , dried		" " dried apple		6.7	2.78
Avocado (pulp)	60	Rat gr.	8.0	8.0	0.97
Banana	18	Rat gr.	3.9	2.9	0.99
"	56	Rat gr.	2.1–2.6		
Berries in human diets	85	Taken as		2.2	0.60
Cantaloupe, fresh	83	Rat gr.	3.0	2.2	0.40
Dates: "Hayany"	94	Rat gr.	5.0	5.0	3.56
" : "Deglet Noor"	94	Rat gr.	2.5	2.5	
Grapes: Malaga	57	Rat gr.	2.6–3.3	3.0	0.96
" : Sultanina	57	Rat gr.	2.6–3.3		
" , canned		Taken as ½ fresh		1.5	1.20

TABLE 21—*Continued*

FOOD	FOOTNOTE	BIOLOGICAL TEST AND OTHER SIGNIFICANT COMMENT	INDEX VALUE IN MGM.-EQ. PER GRAM: Yielded by these data	INDEX VALUE IN MGM.-EQ. PER GRAM: Chosen for this food	CALORIE INDEX: CAL./GM.
			mgm.-eq.	*mgm.-eq.*	
Fruits—Concluded:					
Hawaiian breadfruit, cooked	82	Rat gr.	4	4	1.21
Lemon, pulp		Same as orange		3.3	0.44
Musk melon		T. a. cantaloupe		2.2	0.40
Orange, pulp	18	Rat gr.	5.6–7.2	5.6	0.51
" juice	34	Pigeon mn.	5.2		
" "	55	Rat gr., n. l. t.	2.2		
" "	58	Rat gr.	2.7–3.3		
" "	35	Rat gr.	3.3		
" "	59	Taken as		3.3	0.43
Papaya, fresh	82	Rat gr.	1.9	1.9	0.44
Peaches, fresh		Same as apples		2.2	0.41
" , canned		Same as apples		2.2	0.47
Pears	55	Rat gr., n. l. t.	1.8		
" , Kiefer, raw	61	Rat gr.	4.2	4.2	0.63
Plantain, raw	62	Rat gr.	2.7	2.7	1.00
Prunes, raw	55	Rat gr., n. l. t.	3.8	3.8	0.82
" , dried	63	Calculated: n. l. t.	14	14	3.11
Raisins		As a dried grape, t. a.		7.0	3.45
Strawberry	85	Taken as		2.2	0.39
Yautia, yellow, raw fruit	62	Rat gr.	8.8–11	7.4	1.43
" , white, raw fruit	62	Rat gr.	4.7–6		
Animal Tissues:					
Beef: heart	93	Pigeon prev.	15	15	2.48
" : brain, cerebrum	93	Pigeon prev.	13		1.20
" , " , cerebellum	93	Pigeon prev.	6.6	10	
" , liver	93	Pigeon prev.	32	32	1.29
" , "	18	Rat gr., n. l. t.	24–28		
" , muscle	93	Pigeon prev.	5.2		
" , "	64	Pigeon prev.	5.2	5	2.00
" , "	18	Rat gr.	5.0		
" , " , "dried beef"	65	Pigeon prev.	10.3	10	1.80
Chicken, liver	66	Calc.	10	10	1.37
" , muscle	66	Same as beef muscle	5	5	1.10
Pork: heart	67	Rat gr.	7.5	7.5	1.30
" : liver	67	Rat gr.	10	10	1.26
" , fresh lean muscle	66	Pigeon prev.	37	37	2.50
" , smoked ham	66	Pigeon prev.	37	37	3.00
" , lean loin chops	68	Taken as		37	2.52
" : Bologna sausage	68	Taken as		36	2.34
" : pork sausage	68	Taken as		24	4.50
" : head	68	Taken as		24	4.42
" : ham, medium, fat	68	Taken as		24	3.00
" : ham, fat	68	Taken as		22	3.50
" : bacon, smoked, med. fat	68	Taken as		18	6.25
" : salt pork	68	Taken as		14	7.10
" : sides	68	Taken as		16	5.34
" : jowl	68	Taken as		11	7.63
" : shoulder	68	Taken as		24	3.56
" : fat: lard	89	Rat gr.	10–12	11	9.00
Sheep: brain	67	Rat gr., n. l. t.	2.6		
" : brain	93	Pigeon prev.	5–9	7.0	1.30
" : muscle, "mutton"		Taken same as beef		5.0	2.00
Veal		Taken as beef muscle		5	1.70

TABLE 21—*Continued*

FOOD	FOOTNOTE	BIOLOGICAL TEST AND OTHER SIGNIFICANT COMMENT	INDEX VALUE IN MGM.-EQ. PER GRAM		CALORIE INDEX: CAL./GM.
			Yielded by these data	Chosen for this food	
			mgm.-eq.	*mgm.-eq.*	
Sea-Foods:					
Clams, fresh	96	Rat gr., less than	1.6	1.0	0.30
Fish, fresh, in human diets		Taken as		4.5	1.00
" , dried, " " "	72	Taken as		8.0	3.50
Haddock, cooked	70	Rat gr.	5.0		0.72
Herring	70	Rat gr. (about)	4.0		1.42
" , smoked	71	Based on water content		8.0	2.90
Oysters, fresh	73	Rat gr.	7.5	7.5	0.56
" , cooked	73	Rat gr. "slight loss"	6.0	6.0	0.75
Eggs:					
Hen's egg: solids comm'l	28	Rat gr.	20–23	20	5.42
" " : whole, edible	28	Rat gr.; solids data	5.7	5.6	1.48
" " : " , "	64	Pigeon prev.	5.5		
" " : yolk, raw	5, 33	Pigeon prev., n. l. t.	6.5		
" " : " , "	18	Rat gr.	9–10	9.5	1.48
" " : " , solids	18	Rat gr.	18–20		
Milk and Milk Products:					
Butter (from cow's milk)	90	Pigeon mn. & calc.	8	8	7.69
Buttermilk (from cow's milk)		Taken as		2.2	0.37
Cheese, kind not stated		Taken as n. l. t.		2	4.17
Cow's Milk: malted	76	Rat gr.	33–38	33	3.89
" " : skimmed, dried	35	Rat gr.	13	13	
" " : " , powder, spray process	75	Pigeon prev.	22–25	22	
Cow's Milk: skimmed, fresh	75	Calc.	2.4		
" " : " , "	34	Pigeon prev.	2.2	2.2	0.37
" " : whole, dried	28	Rat gr.	20–23	20	5.08
" " : " , "	78	Rat gr.	20–23	20	5.08
" " : " , "	34	Pigeon prev.	13		
" " : " , fresh	28	Calc. from solids	3.6–4.1		
" " : " , "	74	Rat gr.	3.6		
" " : " , "	35	Rat gr.	3.6	3.6	0.69
Cream, as purchased	92	Calc.		4.2	2.0
Human Milk: American women	77	Rat gr.	2.4	2.4	0.62
Miscellaneous:					
Honey	84	Rat gr.	0	0	3.26
" , comb	84	Rat gr.	0	0	3.00
Molasses: cane	69	Rat gr., n. l. t.	150	150	2.87
" , beet	69	Rat gr.	29	29	2.87
" , sorghum	69	Rat gr.	19	19	2.87
Sugar cane juice	82	Rat gr.	0	0	1.00
Special Vitamin B Preparations:					
From liver:					
"Liver 343 (Lilly) powder"	53	Pigeon mn.	107	110	
From rice polishings:					
"Tiki-tiki"	53	Pigeon mn.	70–80	75	
International standard adsorbate.	53	Pigeon mn. and cure av.	1979	2,000	
"Adsorbed Vitamin B (Lilly) 889071-C"	53	Pigeon mn.	4500–5000	4,500	
Vitamin B_1 Extract, Sterile Solution (P-27034) (for parenteral admin.)	53	Pigeon mn.	1000–1100	1,000	

TABLE 21—*Continued*

FOOD	FOOTNOTE	BIOLOGICAL TEST AND OTHER SIGNIFICANT COMMENT	INDEX VALUE IN MGM.-EQ. PER GRAM: Yielded by these data	INDEX VALUE IN MGM.-EQ. PER GRAM: Chosen for this food	CALORIE INDEX: CAL./GM.
			mgm.-eq.	*mgm.-eq.*	
Special Vitamin B Preparations— Concluded:					
From wheat germ:					
"Bemax"	3	Pigeon mn.	124	130	3.75
"	53	Pigeon mn.	136		
"Embo"	97	Rat gr.	132		3.75
"Vitavose"	53	Pigeon mn.	68		3.72
Yeast and Yeast Preparations:					
Yeast, bakery, dried	3	Pigeon mn.	66		
" , " , " no. 2948	80	Rat gr.	93–133		
" , " , " " 2938	80	Rat gr.	70–100		
" , " , " " 1	81	Pigeon mn.	122		
" , " , " " 2	81	Pigeon mn.	90–100		
" , " , "	60	Rat gr.	96		
" , " , "	78	Rat gr.	48		
Yeast, brewery, dried	28	Rat gr.	180–200		
" , " , " no. 2839	80	Rat gr.; excellent value	?		
" , " , " " 2821	80	Rat gr.	35–50		
" , " , "	15	Rat gr.	200		
" , " , "	81	Pigeon mn.	250–300		
" , " , " autolysed, "Marmite"	3	Pigeon mn.	134	130	
Yeast, dried	47	Rat gr.	200		
" , "	53	Pigeon mn.	100–113		
Yeast Vitamin Powder (Harris) lot 985	19	Taken as standard.		1,000	

Sources of Data Used in Calculation of Vitamin Index Values

Footnote Number

1 Santos and Collado, 1926.
2 Ghose, 1922.
3 Plimmer, Raymond and Lowndes, 1931.
4 Steenbock, Kent and Gross, 1918.
5 Cooper, 1912.
6 Osborne and Mendel, 1920a.
7 McCarrison, 1926.
8 Croll and Mendel, 1925.
9 Indiana Agri. Exp. Sta. Report, 1924.
10 Assumed to be essentially whole corn.
11 Assumed to be essentially whole corn with some bran and germ removed.
12 From composition of whole corn and assumed index values for germ and bran given in table.
13 Assumed to be whole corn with one-half of vitamin lost by canning and dilution with water.
14 McCollum and Davies, 1915.
15 Munsell, 1929.
16 Rose, Vahlteich, Funnell and Macleod, 1932.
17 Osborne and Mendel, 1919b.
18 Roscoe, 1931b.
19 Cowgill, Deuel, Jr., Smith, Klotz and Beard, 1932.
20 Cramer and Mottram, 1927; data in their table II used assuming that wheat germ has an index of 135.
21 Sherman and Axtmayer, 1927.
22 Eddy, 1924.

TABLE 21—*Continued*

23 Miller and Hair, 1928.
24 Hawk, Smith and Bergeim, 1921.
25 Assumed to be like wheat flour.
26 Axtmayer, 1930.
27 Plimmer, Raymond and Lowndes, 1929.
28 Osborne and Mendel, 1919a.
29 Eddy, Kohman and Halliday, 1926.
30 Assuming original value of 20 and loss of one-half the vitamin through cooking and dilution with water.
31 Same as for legumes in general.
32 Cajori, 1920.
33 Salmon and Livingston, 1925.
34 Plimmer, Raymond and Lowndes, 1931.
35 Morgan and Francis, 1924a. See their table 2.
36 Osborne and Mendel, 1922.
37 Same as for turnips.
38 House, Nelson and Haber, 1930.
39 Dunham, 1921.
40 Assuming loss of 24 percent due to boiling; reference 39.
41 Lyman and Blystone, 1926.
42 Based on data of Lyman and Blystone, 1926.
43 Morgan, 1924.
44 80 percent of value for cooked white potato.
45 Miller, 1929.
46 Roscoe, 1930.
47 Miller and Abel, 1933.
48 This is about the lowest value for fruits and vegetables yielded by good tests.
49 Burton, 1928.
50 Same as pumpkins. Pickles are given one-half this value.
51 Rogers, 1928. Also Hessler and Rogers, 1929.
52 Eddy, Kohman and Halliday, 1925.
53 Cowgill, unpublished data.
54 McLaughlin, 1929.
55 Osborne and Mendel, 1920b.
56 Eddy and Kellogg, 1927.
57 Daniel and Munsell, 1932.
58 Sherman and Gloy, 1927.
59 In view of these variable results, the selection has been based on Morgan's comparison of orange juice with milk, for which an accurate index value is available. Roscoe's test was made with the orange pulp; it is possible that this contains more vitamin B than the juice. The value 3.3 seems to be a fair, conservative figure to select for the edible part of the orange.
60 Weatherby and Waterman, 1928.
61 Kansas Agri. Exp. Sta., 1927–28.
62 Cook and Quinn, 1928.
63 Estimated from the difference in water content.
64 Hoagland, 1924.
65 Hoagland, 1929.
66 Hoagland and Lee, 1924.
67 Osborne and Mendel, 1918.
68 The high vitamin content of pig muscle and the relatively large amounts used in various human dietaries make it advisable to estimate index values for the different products which contain muscle. The calculations given here are based upon the assumption that the vitamin occurs chiefly in the nitrogen-containing part of the tissue. As a reference, lean pig muscle, having an index value of 37 and a protein content of 20 per cent (N x 6.25), is taken. For example, pork sausage has about 13 per cent protein. Therefore 20:13::37:x. X calculates to be about 24.
69 Nelson, Heller and Fulmer, 1925.
70 Kik and McCollum, 1928.
71 Assuming water contents of fresh and smoked herring to be 73 and 35 percent respectively (U. S. Dept. Agri., Bull. 28, 1902).
72 The index for fresh herring (Kik and McCollum, 1928) calculates as about 4. Assuming that about 50 percent water is lost in ordinary drying (U. S. Dept. Agri. Bull. 28) dried fish should have an index of about 8. As the index for fresh fish in human diets, kind of fish not specified, I have averaged the values for fresh haddock and fresh herring, thus getting 4.5.
73 Jones, Murphy and Nelson, 1928a.
74 Outhouse, Macy, Brekke and Graham, 1927, paper IV.
75 Johnson and Hooper, 1921.
76 Quinn and Brabec, 1930.
77 Macy, Outhouse, Graham and Long, 1927, paper III.

TABLE 21—*Concluded*

78 Tests by W. H. Eddy for C. P. Wilson: personal communication.
79 Quinn, Burtis and Milner, 1927.
80 Quinn, Whalen and Hartley, 1930.
81 Scheunert and Schieblich, 1929.
82 Miller, C. D., 1929.
83 Newton, 1928.
84 Kifer and Munsell, 1929.
85 Taken same as lowest known vitamin value for this type of food.
86 Hartwell, 1924.
87 According to Oshima (1905), "Takuwan" is a partially dried radish pickled with rice bran. Miller and Abel—see no. 47—have shown that pickling of chinese cabbage in rice bran increases its vitamin B content from 5 to 6 times. Therefore the index for takuwan is taken as 5 times that of radish, or 30.
88 According to Oshima (1905): "Several species of the Allium group are used as food in Japan. One is *Allium fistulosum* which, in form, is more like the leek than the common onion . . . but the kind most commonly used, and the one to which the name onion is generally applied as *A. fistulosum*, mentioned above."
89 Evans and Lepkovsky, 1929. See discussion page 96.
90 Calculated from the values for whole milk and skimmed milk, and correcting for water and salt present in commercial butter. Also assayed on pigeons by Cowgill (unpublished). See discussion, p. 97.
91 Sherman, H. E., 1929. It is not possible to calculate an index from the data submitted, but the statement is made that the bean curd contains almost all the vitamin B of the original soybean used in its manufacture. Assuming the soybean to have an index of 26, it appears safe to assign to the bean curd a value of 20.
92 Calculated on assumption that vitamin is evenly distributed throughout solids of milk, and allowing for respective water contents of whole milk (87 percent) and cream as purchased (74 percent).
93 Cooper, 1914.
94 Smith, M. C., 1928.
95 Aykroyd, 1932.
96 Jones, Murphy and Nelson, 1928b.
97 From assay data—Sherman rat method—submitted by Research Laboratories of General Mills, Inc., through the courtesy of R. C. Sherwood.

polishings is subject to considerable variation depending upon whether the material is fresh or has been stored for a period (West and Cruz, 1933).

Nuts are somewhat variable, ranging from hazel nut and the filbert with an index of 40 through the almond, chestnut and pecan with values approximating 20, to the black walnut with a value of 13.

Most fruits and vegetables have relatively low values. This is contrary to the popular notion that the salad dishes are excellent sources of vitamin B. In all probability the explanation resides in the fact that many of the assays of these foods for vitamin B content have been made on the dried product; when allowance is made for the high water content characterizing the natural food, the index for the food as eaten by man becomes very low in these instances. This should not be construed as indicating that these foods have a low place in the human dietary. The salad dishes constitute valuable sources of the antiscorbutic vitamin; and, to the extent that the leafy portions of plants are used in them, they

contribute notable quantities of vitamin A. Therefore, although these foods are low in content of the B vitamin, they do serve as good sources of the other members of the vitamin group.

There are a sufficient number of vegetables of reasonably high vitamin content to make it unwise to employ any average index value for vegetables as a group unless absolutely necessary. For example, asparagus, artichoke, leeks and parsnips all have index values of 10 or 14. This is in marked contrast to other root vegetables such as onions and turnips, which have such low ratings as 2.7 and 2.4, respectively. Tests of the potato, which constitutes such a large part of many dietaries, have yielded quite variable results ranging from as high as 8 to as low as 3.8 for the cooked product. The value finally selected for this food is 3.8. Even a value as low as this can be significant in the case of a food which is easily eaten by man in large quantities, as can readily be seen upon examination of numerous dietaries presented elsewhere in this monograph (see Chapter XIII).

Another tuber widely used as a food by man is taro. This might almost be said to replace the potato in many of the dietaries in use throughout the Pacific basin. Miller's (1927) assay of this food results in an index value as high as 7. Calculation of the vitamin B content of numerous Japanese dietaries indicates that taro is one of the very important foods serving to make these diets adequate and thus protective against beriberi. Similarly should be mentioned the radish, which, in the form of a pickle, constitutes one of the most common articles of food in Japan; the relatively high index value, 6.2, of this vegetable makes it especially valuable where much polished rice is consumed.

The outstanding point of interest with respect to the vitamin content of animal tissues relates to the unusually high index for pig muscle, or pork. The assays performed by Hoagland were made on both pigeons and rats and led to the same result. According to our calculations lean pork has an index of 37 in contrast to about 5 for beef muscle. According to the growth curves of rats studied by Evans and Lepkovsky (1929) one is justified in assigning to lard a vitamin index of 11. Two interpretations may be placed on this finding. One may consider that some vitamin B is actually present in the lard. On the other hand, one may interpret the data as

Evans and Lepkovsky have done, as indicating that vitamin B is not required in the metabolism of fat, and when this foodstuff is metabolized in large quantities the amount of vitamin required is much less; thus fat acts to "spare vitamin B." This lowering of the amount of vitamin which must be supplied in the food may be regarded as equivalent to supplying a certain amount of the vitamin.

My own vitamin B assays of lard and other fats by the pigeon-maintenance technique are as yet inconclusive with regard to the correctness of one or the other of these two possible points of view. A conservative interpretation of them favors the attitude of Evans and Lepkovsky. My experiments justify an index of only 8 for butter as compared with 11 for lard. This is in harmony with the observation of Evans and Lepkovsky that different fats vary with respect to their vitamin B-sparing potency.

In my opinion the idea that vitamin B may be present in fat cannot be rejected as completely untenable. It is conceivable that the vitamin can exist in such a chemical form as to render it soluble in fats and materials which dissolve fat. Van Veen (1932b) has shown that this antineuritic substance reacts similarly to the better known organic bases, and therefore, should be soluble in organic solvents when present as the free base, and insoluble in these when present as a salt. By an application of this principle Block and Cowgill (1932c) succeeded in extracting large amounts of vitamin B from rice polishings and yeast by use of ether and other organic solvents. Such a result was directly contrary to those reported in earlier literature which seemed to prove conclusively that vitamin B is insoluble in ether. In view of these recent developments one is justified in believing that the so-called "vitamin-sparing action of fats" may after all prove to be due to the actual presence of vitamin B in the fat.

There are instances in the beriberi literature where "fat" was remarkably effective in curing epidemics. Whether the fat actually furnished vitamin B or acted simply to spare this dietary essential is immaterial so far as its value in curing the epidemic is concerned. If the sparing action, as expressed in terms of "equivalence of vitamin," was great enough, a cure could readily result.

One is at a loss to explain why the oyster should have an index

value as high as 7.5, whereas the index for the fresh clam must be less than 1.6, the value for polished rice. Study of the literature indicates that only a few seafoods have been assayed for vitamin B.

The index for whole cow's milk is 3.6. This may seem to be a very low value. One should bear in mind, however, that it is much easier to ingest large quantities of a fluid food such as milk than to eat an equivalent weight of almost any solid nutrient. The practical importance of this is readily illustrated. According to formula 24, page 78, the daily vitamin B requirement of a normal man weighing 70 kgm. (154 lbs.) and having a daily energy exchange of 2500 Calories, would be 4,650 mgm.-equivalents of our test powder. If this man drinks a pint of milk—473 cc.—he obtains thereby 1,703 mgm.-equivalents of vitamin, or 37 percent of his daily requirement.

The high vitamin content of molasses is worthy of comment. This food constitutes one of the few components of the dietary of poor negroes in the Southern States. Examination of such diets as are available (Chapter XIII, pp. 189) shows that the failure of beriberi to appear among the individuals subsisting upon them is to be attributed to three vitamin-rich foods, namely, low-grade corn meal (consisting essentially of the entire maize kernel), pork, and molasses.

From the index values for yeasts listed in Table 21 it is evident that the vitamin content of the yeast plant is quite variable. The values given in the table harmonize with the well known fact that brewery yeasts are usually much better than bakery yeast. This great variability in vitamin B content of yeast in all probability accounts for much of the disagreement in results reported from different laboratories, and also for the frequent failures of investigators preparing yeast vitamin B concentrates to secure a uniform product; presumably the yeasts, from which the concentrates were prepared, varied markedly in content of the vitamin, some being quite rich, in contrast to others which were very poor in this respect.

CHAPTER X

HOW DO THE RATINGS OF FOODS GIVEN IN TABLE 21 COMPARE WITH THOSE OFFERED BY OTHER INVESTIGATORS?

Comparison with Results Reported by Sherman and Associates

IN TABLE XVIII of the *Laboratory Handbook for Dietetics* by M. S. Rose, are given the vitamin B contents of certain foods in terms of the number of Chase-Sherman (Chase, 1928) units per ounce of food. These values have been recalculated to give units per gram and the results incorporated in Table 22 (see column 2). In column 3 of this table are shown the index values finally selected for these same foods, after consideration of all of the data available; these values are taken from the next to last column of Table 21. Comparison of the Chase-Sherman data with our index values is facilitated by inspection of the figures in column 4 of Table 22. These figures are simply the values of the ratio of our index to the Chase-Sherman unitage. The extent to which the values in the last column agree affords some indication as to how our index values agree with the ratings as given with Chase-Sherman units.

In general the two lists agree very well. The average of the values in the last column is 9.74 ± 1.54. The instances where the values are quite different from this average merit comment. In the case of raw egg yolk, the Chase-Sherman list gives this food a much higher rating than does our list. When compared with the data of Roscoe (1930, 1931a, b) and Plimmer, Raymond and Lowndes (1929, 1931, 1933) our rating agrees in indicating that the vitamin B content of raw egg yolk is not as great as the Chase-Sherman value suggests. Tomato is also listed much higher by the Chase-Sherman rating than by ours. Here also we find our own assays made on pigeons agreeing very well with those of Roscoe and therefore are led to conclude that there is ample justification for our

TABLE 22

Comparison of the Index Values Given in Table 21 with Chase-Sherman Unitage for the Same Foods

FOOD	CHASE-SHERMAN VITAMIN B UNITS PER GRAM	MILLIGRAM-EQUIVALENTS PER GRAM OF FOOD. SEE TABLE 21	RATIO OF VALUE IN COLUMN 3 TO THAT IN COLUMN 2
(1)	(2)	(3)	(4)
Apples, fresh	0.282	2.2	7.8
Banana, fresh	0.282	2.9	10.3
Bean, string, fresh	0.317	3.1	9.78
Cantaloupe	0.282	2.2	7.8
Cabbage, fresh	0.493	4.0	8.12
Carrots, fresh	0.282	3.7	13.1
Collards, raw	1.092	11.0	10.1
Eggs, whole	0.564	5.5	9.75
Egg yolk, raw	1.76	9.5	5.4
Flour, whole wheat	2.18	20.0	9.17
Flour, graham	2.18	20.0	9.17
Lemon juice	0.317	3.3	10.4
Lettuce, fresh	0.388	4.2	10.8
Milk, whole fresh	0.317	3.6	11.36
Muskmelon	0.282	2.2	7.8
Oats, rolled	2.18	22.0	10.1
Onions, fresh	0.211	2.7	12.8
Orange juice	0.317	3.3	10.4
Peas, green	2.11	21.0	10.0
Peaches, fresh	0.282	2.2	7.8
Potatoes, white cooked	0.282	3.8	13.5
Peppers, green	0.211	2.2	10.4
Rutabagas	0.282	2.4	8.51
Spinach, fresh	0.775	11.0	14.2
Prunes, dried	1.34	14.0	10.4
Tomato	0.423	2.7	6.38
Turnip greens	1.233	11.0	8.92
Turnip, fresh	0.282	2.4	8.51
Average			9.74
Average deviation			1.54
Average deviation in percent mean			15.8%
Standard deviation			2.01
Standard deviation in percent mean			26.0%

rating. With respect to fresh spinach and cooked white potato it appears that we give these foods higher values than are represented by the Chase-Sherman units. As shown in Table 23, our index

selected for potato is almost identical with that yielded by Roscoe's data; because of our quite uniform agreement with the results of Roscoe's experiments, we feel justified in our choice. Our lack of agreement with respect to raw spinach is probably of no consequence, because this food is always cooked before being eaten by man, and the studies of Rogers indicate very clearly that a marked loss of vitamin B occurs when spinach is cooked or canned. The values of our index given to cantaloupe and muskmelon are subject to considerable error. Data from the assay of cantaloupe indicate that the value must be less than 3, and we do not know how much less it should be. The value selected, therefore, is that found to be the lowest in the many carefully conducted assays of fruits and vegetables; it is quite possible that the true value is closer to 3 than the minimum of 2.2 which was assigned.

Perhaps the failure to give good agreement in these food ratings by the two different units is due in part to the way the growth curves of the rats used in the assays were interpreted. In using the Sherman method of assay, the minimum amount of food taken in estimating the unit is that which allows slight growth in the period of 8 weeks. Comparison of many of the curves in the literature with the interpretation given in the reports describing them indicates in some instances that the unit quantity of food allowed quite appreciable growth; in using these curves for calculating our index we have taken that quantity which allowed just maintenance, feeling that in so doing the results of such estimations would be more comparable with our data obtained from different species.

Comparison with Results Obtained by the Roscoe Technique

Roscoe (1931b) has published the results of many assays of foods for vitamin B and given the foods in the order of their value as source of vitamin B. Table 23 presents such a list. In columns 4 and 5 of this table are shown the index values obtained for these foods if one employs our methods described on page 80 *et seq*; in column 6 are presented the index values finally selected for the foods after due consideration of all the data available in the literature. With certain of the foods (those in column 5 indicated by a dagger) the amount of fresh material equivalent to the dry substance tested is not given, and therefore it has been necessary to estimate the

index from the probable water content of this food. As described below, this may involve a great error. This may account in part for the differences observed with respect to these foods. The

TABLE 23

Comparison of the Index Values Given in Table 21 with the Roscoe Ratings of the Same Foods

FOOD	ROSCOE DATA:* DAILY DOSE NEEDED TO PROMOTE GAIN IN WEIGHT OF 50–60 GRAMS IN 5 WEEKS		INDEX VALUE YIELDED BY THE ROSCOE DATA		INDEX VALUE SELECTED FOR THE NATURAL FOOD. SEE TABLE 21	RATIO: (5)/(6)
	Dry weight	Wet weight	Dry weight	Wet weight		
(1)	(2)	(3)	(4)	(5)	(6)	(7)
	grams	*grams*	*grams*	*grams*		
Yeast, brewery..	0.05	0.25	180–200	....	180–200	1.00
Wheat germ.....	0.1	....	120–140	....	135	0.96
Liver, ox........	0.5	Not given	Greater than 24–28	?	32	......
Watercress......	0.3	Not given	71	7.1†	5.5	1.29
Lettuce.........	0.3	Not given	60	6.6†	4.2	1.57
Orange pulp....	0.25	2.5–5.0	64	6.4	5.6	1.14
Cabbage, etiolated........	0.3 –0.5	Not given	33–40	3.6†	4.0	0.90
Carrot..........	0.25–0.5	2.5–5.0	44	4.9	3.7	1.33
Spinach.........	0.5	5.0	40	4.0	Cooked: 2.4	......
Cabbage, green..	0.95	Not given	35	3.9†	3.5	1.11
Turnip.........	0.5	7.0	34	2.4	2.4	1.00
Tomato pulp....	0.5–1.0	6.25–12.5	28	2.2	2.7	0.81
Egg yolk........	1.0	2.0	20	10.0	9.5	1.05
Onion..........	0.5–1.0	Not given	22	2.7†	2.6	1.04
Meat (ox muscle).......	1.0–1.5	1.0–4.0	20	5.0	5.0	1.00
Banana.........	1.0	4.6	18	3.9	2.9	1.34
Potato..........	1.0–2.0	5.0–10	18	3.6	Cooked: 3.8	......
Apple..........	1.0–2.0	5.5–11	13	2.2	2.2	1.00
						av. 1.10
Average deviation..						0.15
Average deviation in percent mean........................						13.6%

* M. H. Roscoe. 1931. See table III, p. 1208.
† Amount of fresh material equivalent to the dry substance tested is not given; this value is therefore estimated from the probable water content.

extent to which our calculations of index value agree with the results of the Roscoe assays may be ascertained by comparison of the figures in columns 5 and 6. As may be seen by inspection of

column 7, the agreement is even better than in the comparison with the assays made by the Sherman technique (Table 22).

Comparisons with Results Obtained by Other Investigators

The assays reported by Plimmer, Raymond and Lowndes in their series of papers (1929, 1931, 1933) were performed on pigeons. The results obtained with foods, which can be fed to birds in reasonable quantity without having to be dried, agree remarkably well with those yielded by assays on the rat. Examples of such nutrients are the whole grains, legumes, and nuts. When fruits, vegetables, and animal tissues, are considered, however, results are not so concordant. This is probably due to the fact that the nutrient under investigation has such a high water content in the natural state, that it is very difficult to feed it in sufficient quantities to the birds to enable one to make an assay and at the same time to secure proper intake of other important dietary components besides vitamin B. The numerous negative tests obtained by Plimmer and associates were doubtless due to failure to feed a vitamin-poor food in large enough quantities. If the food is dried and tested on either the rat or the pigeon, it is very important to know exactly how much of the dried material represents the original natural food. One cannot assume that the drying process has removed all of the water and proceed on this assumption to a calculation. It is a well known fact that many foods, which have had all water removed by heating to about 105°C., for an appropriate period, absorb some moisture from the atmosphere, when removed from the drying oven; this dried material therefore, when fed to animals in vitamin B assays, really contains appreciable quantities of water. The amount of moisture present varies with different foods. It is obvious, therefore, that the estimation of the proper index for the *natural food* from an assay made with the dried material may involve considerable error. This no doubt accounts for some of the failure of the rat and pigeon assays to agree.

There is also the possibility, particularly in the case of animal tissues, that the vitamin content varies appreciably. In the case of the liver, for example, Osborne and Mendel (1923) showed that the amount of vitamin B present in a unit weight of the organ can be affected appreciably by altering the vitamin content of the diet

with which the animal is fed. In other words, the liver may act as a storehouse for the vitamin and its store may vary in accordance with the supply.

Relative Values of Different Vitamin B Units

The validity of the results of our animal tests, and the relationships of various vitamin B units which they suggest, are supported by a comparison of our findings with those published by Van Veen (1932). According to this investigator, 1 gram of the Jansen-Donath adsorbate contains 100 International Vitamin B Units, and this amount of material is equal to 0.4 mgm. (400 micrograms) of the crystalline vitamin (Jansen and Donath, 1927). From this it follows that 1 International Unit equals 4 micrograms of "pure" vitamin. On page 195 of his paper Van Veen (1932) reports that rice birds—bondols—need 0.4 to 0.5 International Units, or 1.6 to 2 micrograms of the "pure" product, and pigeons require daily from 2 to 3 International Units (20 to 30 mgm. of the adsorbate) or 8 to 12 micrograms of crystalline vitamin; young rats weighing less than 100 grams are reported as needing daily from 1 to 2 International Units, or 4 to 8 micrograms.

According to Table 12 (page 63) a 300 gram pigeon needs daily about 50 mgm. of our standard test powder; our own assays indicate that 20 mgm. of this powder are equivalent to 1 International Unit. Therefore 300 gram pigeons, the standard size for our pigeon unit, receive daily the equivalent of 2 to 3 International Units, which agrees with the Van Veen data.

With respect to the rat, reference to Table 12 (page 63) indicates that a rat weighing 97 grams needs 20 mgm. of our test powder daily, or 1 International Unit. This agrees with the broad statement of Van Veen's results cited above. Van Veen gives data (page 192 of his report) showing that a rat weighing about 42 grams needs daily about 3 micrograms of pure vitamin, or 0.75 International Unit. This result suggests that for rats weighing approximately 50 grams, which is the weight of most of the animals used in the Sherman assay, about 16 mgm. of our test powder would be needed daily. The Van Veen experiment cited above involved *injection of a big dose of vitamin* the effect of which lasted 17 days. The experiments of Cowgill, Deuel and Smith (1925) indicate that

when the minimum dose is given daily instead of single large doses at intervals, the minimum amount required calculates to be about two-thirds of the value obtained by the single-dose method. There-

TABLE 24
Approximate Equivalents of Various Vitamin B (B_1) Units

UNIT	EQUIVALENTS
1 International Unit*	4 Micrograms Jansen-Donath Crystalline Vitamin 1 Roscoe Unit 4 Sherman *et al.* Units 20 Milligram-Equivalents (Cowgill)
1 Microgram Jansen-Donath Crystalline Vitamin†	0.25 International Unit 0.25 Roscoe Unit 1 Sherman *et al.* Unit 5 Milligram-Equivalents (Cowgill)
1 Roscoe Unit‡	1 International Unit 4 Micrograms Jansen-Donath Crystalline Vitamin 4 Sherman *et al.* Units 20 Milligram-Equivalents (Cowgill)
1 Sherman *et al.* Unit§	0.25 International Unit 1 Microgram Jansen-Donath Crystalline Vitamin 0.25 Roscoe Unit 5 Milligram-Equivalents (Cowgill)
1 Milligram-Equivalent (Cowgill)¶	0.05 International Unit 0.2 Microgram Jansen-Donath Crystalline Vitamin 0.05 Roscoe Unit 0.2 Sherman *et al.* Unit
1 Pigeon Unit (Cowgill Weight-Maintenance Technique)‖ *Also* 1 Pigeon Unit (Peters Curative Technique)**	2.5 International Units 10 Micrograms Jansen-Donath Crystalline Vitamin 2.5 Roscoe Units 10 Sherman *et al.* Units

* Vitamins—A Survey of Present Knowledge. Med. Research Council, Spec. Rept. Series, No. 167, 1932. See Appendix II, pp. 313–319.
† Van Veen, 1932.
‡ Roscoe, 1931.
§ Sherman and Spohn, 1923; also Chase, 1928.
¶ Table 21, p. 87.
‖ Block, Cowgill and Klotz, 1932.
** Kinnersley and Peters, 1925.

fore the 50 gram rats commonly used in assays with this species would need daily about 10 mgm. of our powder; this is very close to

what was actually used—8 to 10 mgm.—in estimating index values from the published data of Sherman and others who used his method.

In Table 24 are presented approximate equivalents of various vitamin B units that have been used. These values are of course subject to the error involved in the biological assay, but, even with this qualification, may be of some assistance when attempting to compare results obtained by the different methods.

CHAPTER XI

VITAMIN B CONTENT OF DIETS ASSOCIATED WITH HUMAN BERIBERI

THE estimates of the vitamin B contents of various human diets about to be discussed were based upon the assumption that lack of vitamin B is the primary etiologic factor in the production of beriberi. A review of the literature bearing on this question is presented in Chapter II.

After having used the index values given in Table 21 to determine the total vitamin content of a given ration, the adequacy of this ration for human beings may be studied in several ways. Equation 24[1]

$$\frac{\mathrm{VIT}_i}{\mathrm{CAL}_i} = 0.0000284\ \mathrm{WEIGHT}_{gm.} \tag{24}$$

may be plotted giving the graph shown in Chart 6, p. 110, where the line OA passes through vitamin minima for various body weights. The value of the ratio of vitamin to calories for the diet in question may be considered in relation to the body weight of the individual or average body weight of the group which subsisted on this ration. If the plot of the data is on a point below line OA, the diet should have allowed beriberi; a position above the line should be associated with absence of the disease.

The two dotted lines in Chart 6 represent the plots obtained when 100 kgm. (215 lbs.) and 120 kgm. (264 lbs.) are taken as the maximum body weights for the human species. It is impossible at present to say that these values should be taken rather than 115 kgm. (256 lbs.), the value which yields line OA. It seems reasonable, therefore, to regard the area between the dotted lines as representing a zone of uncertainty. Values for a given diet which fall within this zone should doubtless classify as "borderline";

1. For a discussion of this expression see Chapter VII, pp. 56, and Chapter VIII, pp. 65.

values definitely above this area should represent adequate rations, and those below should be associated with beriberi, these representing diets deficient in vitamin B content.

Another way by which one may express the adequacy of the vitamin content of the ration in question, consists in ascertaining the body weight for which the diet would be just barely satisfactory and comparing this weight with that of the individual or group which ate this ration. A third method consists in calculating the amount of vitamin which an individual of the appropriate weight would obtain if he ate of the diet in question in amount sufficient to satisfy his energy requirement.

All of these ways of approaching the problem necessarily give the same result because they are based upon the fundamental relationship expressed in equation 24. They differ somewhat, perhaps, in their usefulness as vehicles for expressing the failure of the diet to satisfy the need for vitamin, or the superiority of the ration in this respect. In the discussions to follow it will be observed that each of these methods is used; the selection of any one in a given instance has been governed solely by the desire to exhibit the adequacy or the shortcomings of the given diet as clearly as possible.

Examination of the literature dealing with beriberi reveals numerous diets that can be studied with respect to their adequacy in vitamin B content. Aykroyd (1930) recorded the foods eaten by 25 families in Newfoundland and Labrador, and Megaw and Bhattacharjee performed a somewhat similar service in Calcutta, India. These will be discussed under a group heading of *Families*. The dietary experiments of (*a*) Wright at the Pudoh Gaol, Selangor, (*b*) Fletcher at the Kuola Lumpur Lunatic Asylum, (*c*) Frazer and Stanton in Java, and (*d*) Strong and Crowell with volunteers from the Bilibid Prison, Manila, were attempts to elucidate the rôle of the diet in the causation of beriberi, and thus form another category of interest. The appearance of beriberi in greater or lesser extent among the inmates of various public institutions, who are restricted to the food offered by the management, is a fact worthy of notice. Although records of the rations used in many such institutions are lacking, a sufficient number of them have been found to make possible a study of the amount of vitamin B present in them.

These have been grouped together for discussion. Beriberi has also occurred in epidemic proportions among the members of military and naval organizations, and the official rations in use when the epidemics appeared are on record. Study of these diets constitutes still another category of interest. The 180 separate combinations of foods, which have been studied for vitamin B content in relation to the development or disappearance of beriberi, have been grouped

TABLE 25

Vitamin B (B_1) Content of the Diets of Families in Newfoundland and Labrador Studied by Aykroyd (1930)

FAMILY NUMBER	FAMILIES IN WHICH BERIBERI OCCURRED		FAMILIES IN WHICH BERIBERI DID NOT OCCUR	
	Vitamin B intake		Vitamin B intake	
	Per person per day	Per calorie per day: $\frac{\text{Vitamin}}{\text{Calories}}$	Per person per day	Per calorie per day: $\frac{\text{Vitamin}}{\text{Calories}}$
	mgm.-eq.		*mgm.-eq.*	
1	4,037	1.44	5,418	2.09
2	3,901	1.55	7,281	2.12
3	3,022	1.53	5,587	2.09
4	5,076	1.91	5,722	2.11
5	7,924	2.16	10,754	1.95
6	6,794	2.37	9,023	3.50
7	4,450	1.85	6,719	2.13
8	6,819	1.76	12,299	2.45
9	6,992	1.48	10,264	2.06
10	5,467	1.81	6,821	1.85
11	8,677	1.57	5,194	1.76
12	4,471	1.63	10,266	2.06
13	3,871	1.56	......	....
Average	5,543	1.74 a.d. 0.22	7,946	2.18 a.d. 0.26
Average omitting family 6	.....	....	7,831	2.06 a.d. 0.11

according to the categories just described. The results of their study will now be presented and discussed.

In Families and Similar Groups in Relation to Incidence of Beriberi

Families in Newfoundland and Labrador: Aykroyd Data

Aykroyd (1930) collected data on the foods eaten by 25 families in Newfoundland and Labrador during a period of six months includ-

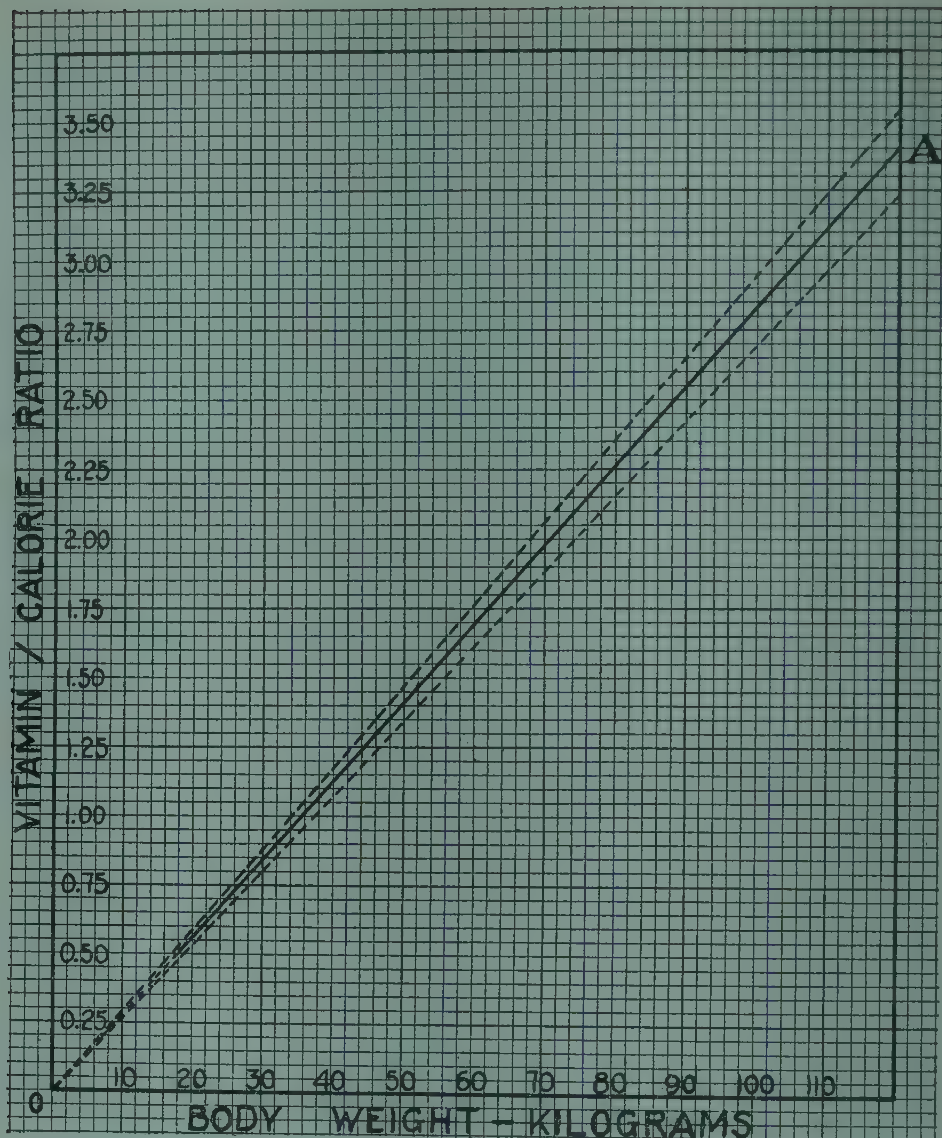

CHART 6

The Human Requirement of Vitamin B (B_1)—Prediction Chart. The adequacy in vitamin B B($_1$) content of a given human diet for individuals of different body weights may be estimated by reference to this chart. The plot indicated by line OA represents the probable minimum vitamin B (B_1) requirement referred to body weight. The area between the dotted lines represents a zone of uncertainty; for discussion of this area see the text. If the Vitamin/Calorie value of the diet for a given body weight falls definitely above line OA, the ration is deemed adequate with respect to vitamin B (B_1); if the plot proves to be appreciably below the line, the vitamin requirement is not satisfied by this diet and beriberi should occur provided the period of subsistence on this ration is sufficiently extended; if the plot is close to line OA, or between the dotted lines, the diet may be considered as "borderline" in character.

ing the winter months of 1928–1929. Beriberi occurred in 13 of these families; the extent to which the disease appeared was not stated. Similar data were obtained for 12 families who ate diets which seemed to be very poor and similar to those in the beriberi group; in all of these 12 families, however, this disease did *not* appear. Here are presented for consideration, therefore, two groups of diets, which upon cursory inspection are practically the same, but which, nevertheless differ in this respect, that one was associated with beriberi and the other was not. How do they compare when their vitamin contents are estimated by means of the food index values given in Table 21? A summary of these data is given in Table 25.

Examination of Table 25 shows average values of the VIT/CAL ratio of 1.74, ±0.22, for the beriberi group, as compared with 2.18, ±0.26, for the non-beriberi families. Family 6 of the latter group appears to have had a much better diet than the others, shown by the high value 3.50; if this case is disregarded, the average for the healthy families calculates as 2.06, ±0.11.

In attempting to interpret these results in terms of average men, the question arises as to what body weight should be taken as representative of the average man in these instances. Aykroyd expresses his results in terms of "per man per day," and, to arrive at this, necessarily made use of conventional factors when considering women and children. As an approach to this problem I have taken 66 kgm. (145 pounds) as the weight of the average man; this is the figure given by Davenport and Love (1921) as the average weight of recruits of English origin[1] in the U. S. Army.

Reference to Chart 6 shows that the minimum value of VIT/CAL for 66 kgm. is 1.87; when this is compared with the average value of 1.76 for the beriberi families of Aykroyd, it appears that these diets should have permitted beriberi to develop. Inspection of the values for the different families reveals that only families 4, 5, 6 and 7, out of the 13 in the group ate rations with values of this ratio greater than the average of 1.76, and in only one of these, No. 6, was the value considerably higher. Inspection of Chart 6 and Table 26 also reveals that the average value of 1.76 is just ade-

1. See Table 110, p. 243, of the work by these authors.

quate for a body weight of 62 kilograms, which suggests that the factor of safety against beriberi was nil, or at least extremely small.

When the data for Group II—the non-beriberi families—are considered in the same way, it appears from the average value of the VIT/CAL ratio of 2.06, that beriberi should not have appeared, and this agrees with the facts. The plot for this value is appreciably above the line indicating vitamin minima. In only one case—family 11—was the value definitely below the line, and in this instance, the value is equal to the average of the beriberi families; family 10 ate a diet having a value falling almost exactly on the line. The average value for the healthy families proves to be just sufficient for a man weighing 73 kgm., according to Table 26.

TABLE 26

Newfoundland and Labrador Families (Aykroyd). Summary Table

PRESENCE OF BERIBERI	VITAMIN B INTAKE DAILY		BODY WEIGHT FOR WHICH THIS INTAKE WOULD BE JUST ADEQUATE (SEE CHART 6)	PROBABLE AVERAGE WEIGHT OF GROUP
	Per man	$\frac{\text{Vit.}}{\text{Cal.}}$		
	grams. eq.		*kgm.*	*kgm.*
Group I. Beriberi was *present*......	5.54	1.76	62	66
Group II. Beriberi was *absent*.....	7.95 7.83*	2.18 2.06*	77 73	66

* Average obtained by omitting consideration of one obviously very good diet. See Table 25.

It is quite possible that I have not selected the proper average weight upon which to base our comparison. Even if this be granted, and the matter be examined from the point of view of a range of body weights over which the comparison might be made, it is evident from Chart 6 that our plotted line indicating predicted minima runs definitely between the two groups of families. Therefore, one may conclude that the data of Aykroyd support the thesis being advanced. The estimations of vitamin content of these diets agree with the facts concerning the incidence of beriberi and the human requirement for vitamin B predicted by our formula.

Calcutta Groups: Megaw and Bhattacharjee Data

A Group of 70 cases was studied by these investigators. Malaria sufficient to account for an intermittent slight fever of 99–100°

occurred as a complication in 13 individuals of this group. Megaw and Bhattacharjee (1924) were able to study 23 cases under carefully controlled conditions and to secure some fairly accurate information as to the diets eaten. In two of the 23 controlled cases vomiting occurred; 20 of this group exhibited a definite loss of appetite, and 11 were also afflicted with diarrhea.

TABLE 27

Dietaries of Groups Among Whom Beriberi Appeared

(Megaw and Bhattacharjee, 1924)

FOOD	VITAMIN INDEX	CAMPBELL HOSTEL		KALA BAGAN GROUP: LABORING HINDUS		PARSIBAZAR GROUP: LABORING MOHAMMEDANS		ANGLO-INDIANS: RAILWAY QUARTERS	
		Amount daily	Vitamin Content	Amount daily	Vitamin Content	Amount daily	Vitamin Content	Amount daily	Vitamin Content
		grams	*mgm.-eq.*	*grams*	*mgm.-eq.*	*grams*	*mgm.-eq.*	*grams*	*mgm.-eq.*
Rice	1.6	200	320	360	576	300	480	120	192
Dhal	23	120	2,760	120	2,760	120	2,760	90	2,070
Fish	4.5	120	540	60	270	60	270	120	540
Vegetables	3	240	720	120	360	120	360	200	600
Bread	2	60	120	...	.....	120	240	240	480
Meat	5	20	100	...	.....	...	.....	120	600
Butter and Ghee	8	10	80	...	.....	...	.....	30	240
Sugar or Sweets	0	240	.....	200	0	200	0	60	0
Fruits	3	...	.....	...	.....	...	.....	120	360
Eggs	5.5	...	.....	...	.....	1	6	2	11
Milk	3.6	...	.....	...	.....	...	.....	480	1,280
Sujee	?	...	.....	...	.....	...	.....	60	?
Totals:									
Vitamin		4,640		3,966		4,116		6,373	
Calories		2,200		1,822		2,100		3,000	
VIT/CAL			2.11		2.18		1.96		2.12

Four diets ingested by these patients and representative of different social classes were cited by these authors. For comparison data were also secured concerning three diets used by persons of similar social status but free from beriberi. Judging from the amounts of the foods stated, these rations, presented in Tables 27 and 28, must be only roughly approximate. It will be noticed

that the quantities of nutrients are given to only two significant figures. The results of the calculations of vitamin contents of these diets, therefore, must be regarded as merely approximate, in contrast, for example, to the data furnished by Aykroyd in his study of the Newfoundland and Labrador families.

In discussing these diets, Megaw and Bhattacharjee expressed the opinion that rice intoxication was not eliminated as a cause of beriberi. It is interesting, therefore, to find, upon application of our

TABLE 28

Dietaries of Calcutta Groups Free From Beriberi

(Megaw and Bhattacharjee, 1924)

	VITAMIN INDEX	WORKING CLASS: MOHAMMEDANS		WORKING CLASS: HINDUS		BENGALI GIRLS: BOARDING SCHOOL	
		Amount daily	Vitamin content	Amount daily	Vitamin content	Amount daily	Vitamin content
		grams	*mgm.-eq.*	*grams*	*mgm.-eq.*	*grams*	*mgm.-eq.*
Rice	1.6	360	576	480	768	180	288
Dhal	23	160	3,680	180	4,140	120	2,760
Vegetables	3	200	600	200	600	200	600
Fish	4.5	30	135	30	135	120	540
Bread	2	60	120	...	.....	60	120
Sugar or Sweets	0	200	0	240	0	210	0
Eggs	5.5	1	6	...	.....	...	.....
Milk	3.6	...	.....	...	.....	120	432
Butter and Ghee	8	...	.....	...	.....	30	240
Totals:							
Vitamin		5,117		5,643		4,980	
Calories		2,180		2,295		2,200	
VIT/CAL			2.35		2.46		2.26

method for estimating vitamin B contents, that the rations shown in Table 27—associated with beriberi—actually contained less vitamin per calorie than those of Table 28, which did not allow the disease to develop. The diet used in a Bengali Girls Boarding School—Table 28, last column—is the only one of the non-beriberi group which approached the diets of Table 27 with respect to value of the VIT/CAL ratio; in this case a lower value of this ratio could still be associated with absence of beriberi because the persons con-

cerned, namely, girls in a boarding school, would be of smaller body weight than the individuals of the other groups under consideration. The average VIT/CAL value for the beriberi group, Table 27, is 2.09, which should be compared with the value 2.36 for the non-beriberi diets in Table 28.

Examination of these rations by our method indicates that their ability or failure to protect against beriberi was due chiefly, but not solely, to the amount of dhal ingested. Not a single one of the diets in Table 27 contained over 120 grams of this food, whereas the dietaries of the two working-class groups in Table 28 contained as much as 160 and 180 grams per day, respectively. McCarrison (1924) has pointed out that the chief focus of beriberi in India is in Madras, where rice is the chief staple food, and, from a study of numerous samples of rice was led to believe that some other factor than rice-eating plays an important rôle; he suggested that a poison of some kind is a causative factor. In view of the results of our method for evaluating diets for their content of vitamin B, applied to the Calcutta rations described by Megaw and Bhattacharjee, is not another explanation more likely? Variations in the kinds and amounts of other foods used to supplement the rice would seem to constitute a simple explanation of his findings. In the absence of any method by which to estimate with reasonable accuracy the vitamin contributions made to a dietary by different foods, the attitude of McCarrison had much to justify it. The results of the use of our method, described thus far, however, support the alternative explanation indicated above.

In Beriberi Experiments on Human Beings

Wright's "Correct and Liberal Diet on Which Convicts Yet Constantly Incurred Beriberi"

H. Wright carried out some experiments at the Pudoh Prison in Selangor during 1901–1902. The possible rôle of fish as a cause of beriberi was studied by feeding a diet from which this food was eliminated. During the experimental period of eleven months no fish of any kind was permitted to enter the prison, and yet, as Braddon describes it, "numerous cases of beriberi continued to occur among the inmates." The ration which was fed during this

period, was described as "a correct and liberal diet." Sufficient details are given to enable us to estimate the vitamin B content of this dietary according to the method described on preceding pages.

The results of a study of Wright's correct and liberal diet are presented in Table 29. It appears that this ration might have been sufficient for some of the men but not for all. Certainly the factor of safety was extremely small. This accords with the fact that the convicts fed this diet "yet constantly incurred beriberi."

TABLE 29

Vitamin B Content of the Diet Used at the Pudoh Gaol, Selangor, Which H. Wright Described as a "Correct and Liberal Diet . . . on Which Convicts Yet Constantly Incurred Beriberi"

(Braddon, 1907, p. 40)

DIETARY COMPONENT	AMOUNT DAILY	VITAMIN INDEX	VITAMIN B CONTENT	CALORIES, APPROXIMATE
	grams		*mgm.-eq.*	
Rice	594	1.6	950	2,085
Meat "butcher's"	170	5	850	340
Vegetables	198	3	594	91
Beans	57	23	1,311	202
Fat (taken as lard)	28	11	308	252
Salt, etc.	42	0	0	0
Totals			4,013	2,970
VIT/CAL ratio			1.35	
Body weight for which this value of the VIT/CAL ratio is just adequate			48 kgm.	
Probable weight of prisoners			40 to 60 kgm.	

Kuala Lumpur Lunatic Asylum: Fletcher's Experiments with Cured (Parboiled) and Uncured Rice, 1905 and 1907

In the Kuala Lumpur Lunatic Asylum during 1905 and 1907, Fletcher (1909) tested Braddon's theory that beriberi is due to the ingestion of too great an amount of uncured, or polished white rice. The diets which he used have been examined with respect to their vitamin B contents. A brief description of the plan followed in these important experiments will serve to indicate their great significance in proving that beriberi is fundamentally a disease dietary in origin.

There were two groups of lunatics housed in exactly similar

buildings on the opposite sides of a quadrangle, surrounded by a high wall. On December 5, 1905, all the inmates at that time in the hospital were given numbers. Those with odd numbers were sent to one ward and given the diet containing uncured or polished white rice. The lunatics with even numbers were sent to the other ward and fed a ration exactly like that given to the other group except with respect to the rice component; in this case the rice was of the cured, or parboiled variety. The foods were prepared by the same cook. The water supply was the same for both groups. After a period of six months, the groups exchanged quarters. This was done as a control against the possibility that the beriberi which appeared was due to infection localized in the living quarters. Experiments of this sort were repeated in 1907.

The results of these tests may be summarized briefly as follows. Excluding all individuals who had been in the asylum less than 28 days, 154 patients were fed on the cured rice diet, and not a single one of these persons developed beriberi; 153 patients received the uncured, or polished rice ration, and of these 65 developed beriberi in the institution. Place infection could not account for these results, because the disease only appeared in the ward where the polished white rice was fed. The possibility of contagion is ruled out by the fact that the lunatics were allowed to associate with each other.

Some observations were made of the effect of feeding the two test diets to persons suffering from the disease. Of the 36 beriberi patients receiving white, polished rice, 24 died, giving a mortality of 66 percent. The mortality rate in a group of 30 patients who were fed with the cured rice was 10 percent.

The results of estimations of the vitamin B contents of these diets are presented in Table 30. The original data do not indicate clearly what kinds of meat were used; because of the relatively high value of pork as compared with beef and other kinds of meat, this is unfortunate. It has been necessary, therefore, to make certain assumptions as to the amounts of beef and pork that were fed. Considering the information available as to the amount of pork eaten daily in other institutions in the Far East, it is estimated that not over 20 grams were consumed daily on an average. In all probability the correct amount was somewhat lower. By taking

this slightly higher figure, however, we increase rather than diminish the vitamin content in our calculations; in the case of the polished rice diet therefore, we make the calculation operate against instead of in support of our favored thesis.

In the estimation of the vitamin B content of the cured rice, an index value as low as 10 has been assumed. It is quite possible that a higher value should have been used; according to Table 21 (p. 87), a value as great as 15 is justified. This would operate to give the ration an even greater factor of safety than is shown by the data in Table 30.

TABLE 30

Vitamin B Contents of Diets Used by Fletcher in His Experiments at the Kuala Lumpur Lunatic Asylum

(Cited by Vedder, 1913, p. 162)

GROUP	DIETARY COMPONENT	AMOUNT DAILY	VITAMIN INDEX	VITAMIN B CONTENT	CALORIES, APPROXIMATE
		grams		*mgm.-eq.*	
I	Rice, white polished	794	1.6	1,270	2,787
II	Rice, cured	794	10 (or 5?)	7,940 (or 3,970?)	2,779
Both	Fresh meat	65			
	(If beef)		5	325	130
	(If 45 grams beef and		5	225	90
	20 grams pork)		24	480	60
	Fresh fish	45	4.5	203	45
	Salt fish	22	8	176	77
	Vegetables	227	3	681	159
	Cocoanut oil	19	8(?)	152(?)	171

	PARTY I—POLISHED RICE GROUP		PARTY II—CURED RICE GROUP		
Total vitamin daily	3,034	3,414	5,734	6,114	9,957
Total calories daily	3,369	3,389	3,361	3,381	3,381
VIT/CAL value	0.90	1.01	1.71	1.81	2.95
Body weight for which this VIT/CAL is adequate	30 kgm.	34 kgm.	60 kgm.	64 kgm.	104 kgm.

According to these estimates (Table 30) the ration with polished, uncured, white rice had a VIT/CAL value of not over 0.96, making it just adequate for men weighing 34 kgm. This diet, therefore, should have allowed many cases of beriberi to develop, which in

fact did occur. The VIT/CAL value of the ration containing cured rice was 2.90, making this diet more than sufficient for the patients; as a matter of fact, not a single healthy person subsisting on this diet developed beriberi. The reader may inquire as to why, therefore, did three beriberi patients die, although given this ration. We have no information as to how much of the diet was really eaten by these unfortunate individuals. Anorexia is a common symptom of the disease. Furthermore, investigators working with animals are well aware that treatment, by feeding a suitable diet of common foods, gives slow improvement in contrast to administration of relatively large doses of the vitamin; even where big doses are given, frequently the animals die because the condition is too advanced to respond to any therapy less than parenteral administration of very concentrated forms of the antineuritic factor.

From this brief consideration of Fletcher's data it is evident that his results, obtained in the Kuala Lumpur Lunatic Asylum, harmonize with the writer's views, and are readily explained by them.

Frazer and Stanton Experiments

The famous experiments of Frazer and Stanton in 1907–1908, which showed conclusively that beriberi was definitely associated with a diet consisting almost entirely of polished rice, have been studied in relation to the problem considered in this monograph. These investigators took 300 Javanese laborers into a virgin jungle, where new and sanitary quarters were built. All cases of beriberi occurring in the group at this time were excluded. The remaining men were then distributed between two parties of equal numbers. The rations given to the two groups were the same except in one respect, namely, party I received white, polished rice as the staple article of food, whereas party II was given parboiled rice. After 89 days the first case of beriberi appeared in party I. When a certain number of cases had been noted, the use of polished rice was discontinued and no new cases appeared thereafter. No beriberi developed in party II, which received parboiled rice instead of the polished variety. The conditions were then reversed, that is to say, the men in party I were now given the diet previously fed to group II, and those in group II were now fed with the ration previously used with party I. Again, after a somewhat longer period, beriberi

appeared among the men eating the polished rice diet, but no cases developed in the group receiving parboiled rice. These carefully controlled experiments established the fact that the appearance of beriberi was associated with a too liberal use of polished rice.

Numerous investigators have obtained the same results in animal experiments. More recently, Aykroyd (1932) has studied the effect on the vitamin B content in rice of the parboiling and milling processes and has demonstrated by tests on rats that parboiled rice

TABLE 31

Vitamin B Contents of the Diets Fed to Parties I and II of the Frazer and Stanton 1907–1908 Experiments

(Frazer and Stanton, 1924)

GROUP	DIETARY COMPONENT	AMOUNT DAILY	VITAMIN INDEX	VITAMIN B CONTENT	CALORIES, APPROXIMATE
		grams		*mgm.-eq.*	
I	White Rice	604	1.6	966	2,120
II	Parboiled Rice	604	10	6,040	2,114
Both	Dried salt fish	120	8	960	420
	Onions	50	2.7	135	25
	Potatoes	50	3.8	190	49
	Cocoanut oil	24	8 (?)	192 (?)	216
	Cocoanut	39	4	156	230
	Tea	3	0	0	0
	Salt	3	0	0	0

	GROUP I	GROUP II
Total vitamin daily	2,599	7,673
Total calories daily	3,060	3,054
Vitamin/Calories	0.85	2.51
Weight for which VIT/CAL just adequate	30 kgm.	88 kgm
Weight of men in these groups	45 kgm.	45 kgm.

is unusually rich in the vitamin. Evidently, the parboiling process results in distribution throughout the endosperm of the vitamin normally located chiefly in the bran and germ parts of the rice kernel. There may be a slight loss of vitamin through diffusion into the water in which the rice is placed when being parboiled.

In Table 31 are presented data with respect to the vitamin B contents of the diets fed to parties I and II of the Frazer and Stanton experiments. As the index to use with parboiled rice a value as low as 10 has been taken, although Table 21 gives 15 as a

fair figure to use. The value of the VIT/CAL ratio in the case of the diet for party I proves to be as low as 0.79; reference to Chart 6 shows that such a low value as this makes the diet just barely adequate for a body weight of about 28 kgm., whereas the average weight of the men is given by Frazer and Stanton as being about 100 pounds, or 45 kgm. Therefore this diet was markedly deficient in vitamin B and should have permitted the development of beriberi, the first case of which appeared in as short a time as 89 days. The ration for party II, which contained parboiled rice, has a VIT/CAL value of 2.45, which would make it adequate for weights up to 86 kgm., or 189 pounds! Even if parboiled rice is given an index value as low as 5, the diet proves to be just adequate with a slight factor of safety for a body weight of 51 kgm.; in this case the VIT/CAL ratio calculates to be 1.46. From these estimations it is quite evident, that beriberi should have appeared in the group fed the polished rice diet, and should have been absent, when parboiled rice, instead, was fed along with other foods indicated in Table 31.

Strong and Crowell Experiments

The feeding experiments, which Strong and Crowell (1912) conducted with volunteers from the Bilibid Prison, Manila, were designed to test the hypothesis that prolonged subsistence on a diet consisting chiefly of white rice results in beriberi. To quote these authors:

> The object of our study was to determine definitely, if possible, whether beriberi, as it occurs in the Philippine Islands, is an infectious disease or whether it is one which has its origin in disturbances in metabolism, brought about by the prolonged use of polished rice as a staple article of diet. The experiments were carried out in Bilibid Prison in which institution the hygienic conditions may be said to be almost ideal. . . . The nature of the experiments having been outlined and the Government having given its sanction to the same, a number of prisoners, under sentence of death, were selected and the nature of the proposed experiments carefully explained to them in their own dialect. They were told that the experiments were for the purpose of testing the comparative value of different kinds of rice as a food; the articles of food comprising the diet that would be given to them were enumerated, and they were also told that perhaps they might contract beriberi. The proposition was stated to them clearly. In addition, they were to be allowed an abundance of cigarettes of any kind that they wished, and also cigars if they desired them. Volunteers were then asked for. Twenty-nine of the number volunteered. The remaining ones

did not care to undertake the experiment. Each of the volunteers then signed a statement, written in his own dialect, stating that he undertook the experiment entirely voluntarily and that he would agree to continue with the experiment until it was completed.

The original plan of the experiment called for distribution of the volunteers among three groups, the first to receive essentially white rice and rice polishings, the second group white rice supplemented by an alcoholic extract of rice polishings, and the third only white rice and the basal diet. Attempts to feed uncooked rice polishings, however, met with failure; these men were then given the basal diet with red rice substituted for the polished product. As finally constituted, the groups were as follows:

Group I. White rice, extract of rice polishings and special diet.
Group II. White rice and special diet.
Group III. Red rice and special diet.
Group IV. White rice and special diet.

The report of the study gives details concerning the physical condition of the volunteers from time to time, and the amounts of the various foods eaten; the quantities of the various nutrients were estimated to the nearest five grams in nearly all instances, and therefore were not as accurate as might be desired. For this reason the calculations of vitamin B furnished by these diets are necessarily subject to greater error than would otherwise be the case. It is particularly unfortunate that the 40 cc. of rice polishings extract, reported as having been given daily, was mixed with the rice offered instead of being administered separately. Inspection of the records of rice intake shows that the amounts of this food taken daily varied considerably. With anorexia usually the first sign of vitamin B deficiency, and the protective substance being mixed with the food offered, it is obvious that a vicious circle is set up, which can only be cut by administering the vitamin apart from the ration. Inasmuch as many workers seeking to prepare suitable extract of vitamin B have reported appreciable variation in the amount of this factor present in different rice polishings, and no animal assays were made of the particular extract used in the Strong and Crowell experiments, it is impossible to say how much vitamin B the men in Group I received from this source. West and Cruz (1933) have shown that rice polishings suffer a loss of vitamin

B during storage unless given special treatment. Furthermore, the vitamin assays of different samples of tikitiki (rice polish extract) by Hermano and Anido (1933) indicate that there is considerable variation in the vitamin B content of such preparations, some containing only very small amounts. The fact that two of the six men in Group I developed beriberi suggests that the extract could not have been very rich in vitamin B. For these reasons no calculations of the vitamin intake of the men in Group I were attempted.

When estimations are made of the vitamin B intake of the men who subsisted largely on white, polished rice (those in Groups II and IV), the data presented in Table 32 are obtained. It will be noticed that, whereas the average value of the vitamin/calorie ratio, expressing the requirement of these men, proves to be about 1.50, the value of the ratio yielded by the food intake data was only 0.83, or about 55 percent of the estimated minimum. Three of the men (Group IV, Nos. 24, 27 and 28) failed to develop beriberi. This may have been due to too short a period of subsistence on the deficient diet, or a better utilization of the limited supply of vitamin by these particular individuals. Investigators working with groups of experimental animals are well aware of differences in the time required for symptoms of vitamin B deficiency to appear in different individuals; occasionally one meets with an animal which fails to show the characteristic manifestations even after unusually long periods. The notes of Strong and Crowell do not state why "it became necessary to change the diet." The fact that each of these men suffered a marked loss in body weight while on the white rice diet, suggests that they were not absolutely unaffected by the vitamin deficiency régime. It will be noticed in Table 32, that prisoners 12 and 7 (Group II) exhibited some of the signs of beriberi but not all, after having been on the polished rice dietary for 108 and 97 days, respectively; both of these periods were longer than those of prisoners 24, 27 and 28. Is it not reasonable, therefore, to believe that if these latter men had continued on the special dietary for an appreciably longer time, they too would have exhibited some, if not all, of the signs of beriberi?

The individuals in Group III subsisted upon a ration the chief component of which was red rice. It is stated[1] that "the term 'white

1. Strong and Crowell, footnote, p. 294.

rice' will be used to indicate the highly polished rice and the term 'red rice' the unpolished rice." Braddon (1907) and Vedder (1913) show, by extensive discussions in their monographs, that unpolished raw rice is usually spoken of as "brown rice," and the parboiled variety is frequently described as "red rice," because of the red color which develops as a result of the parboiling process. It has been assumed, therefore, that the red rice used in the Strong and Crowell experiments was a rice that had been parboiled but not milled, and therefore it should probably be given a vitamin index

TABLE 32

Vitamin B Contents of Diets Used by Strong and Crowell (1912) Volunteers, Groups II and IV, Consisting of White Rice and a Special Supplementing Diet Low in Vitamin B

GROUP	PRISONER NUMBER	BODY WEIGHT DURING EXPERIMENT—AVERAGE	VITAMIN/CALORIE RATIO		NUMBER OF DAYS ON THE DIET	DID BERIBERI APPEAR?
			Yielded by food intake data	Needed for the given body weight		
		kgm.				
II	7	57.1	0.97	1.61	97	Some signs, but not all
	8	56.5	0.82	1.60	97	Beriberi
	9	53.2	0.82	1.50	97	Beriberi
	10	43.6	0.84	1.22	108	Beriberi
	11	52.9	0.78	1.50	97	Beriberi
	12	56.4	0.82	1.60	108	Some signs, but not all
	Average...	53.3	0.84	1.50		
IV	19	45.2	0.80	1.28	92	Only early signs
	20	42.6	0.79	1.20	92	Beriberi
	21	51.1	0.83	1.44	92	Doubtful signs
	22	55.5	0.85	1.57	92	Early signs
	23	59.7	0.82	1.67	92	Only edema in legs
	24	54.1	0.83	1.53	92	No beriberi; only weight loss
	25	57.8	0.86	1.64	81	Beriberi
	26	61.9	0.83	1.76	81	Beriberi
	27	45.6	0.83	1.29	82	No beriberi; only weight loss
	28	47.2	0.79	1.33	82	No beriberi; only weight loss
	29	50.1	0.82	1.42	75	Beriberi
	Average...	51.9	0.82	1.47		

value of about 15 for these calculations. Owing to the fact that vitamin B assays of different samples and kinds of rice have shown that marked variations in vitamin content do occur (Vedder and Feliciano, 1928; Aykroyd, 1932; Acton, Ghosh and Dutt, 1933; Ghosh and Dutt, 1933; Van Veen, 1933), estimates were also made, based upon the assumption that the index for this red rice should be 5 and 10, respectively. The results of the calculations are summarized in Table 33.

TABLE 33

Vitamin B Intakes of Strong and Crowell (1912) Volunteers whose Diet Consisted of Red Rice and a Special Supplementing Ration Low in Vitamin B

GROUP	PRISONER NUMBER	AVERAGE BODY WEIGHT DURING EXPERIMENT	VITAMIN/CALORIE RATIO				NUMBER OF DAYS ON THE DIET	DID BERIBERI APPEAR?
			Needed for the given body weight	Yielded by food-intake data, assuming vitamin index of red rice to be				
				5	10	15		
		kgm.						
III	13	50.8	1.43	1.61	2.68	3.75	100	Rather marked symptoms
	14	53.4	1.50	1.59	2.70	3.81	80	No beriberi; only weight loss
	15	51.4	1.44	1.60	2.68	3.76	100	No beriberi; only weight loss
	16	59.3	1.66	1.60	2.69	3.78	100	No beriberi; only weight loss
	17	51.8	1.46	1.59	2.68	3.77	100	No beriberi; only weight loss
	18	55.0	1.56	1.59	2.69	3.79	100	Slight cardiac symptoms
	Average...	53.6	1.53	1.60	2.69	3.78		

Two of the six men in Group III developed some of the symptoms of beriberi; the remaining four prisoners were free from the disease, but did show some loss in body weight. The fact that beriberi appeared in two members of this group has been emphasized (Megaw, Findlay, *et al.*, 1930) as constituting evidence against the theory that beriberi is due to a dietetic deficiency. The data in Table 33 indicate that with vitamin index values for red rice ranging from 5 to 15, the diets should have furnished sufficient vitamin B; where an index of 5 was used, the amount of vitamin furnished was just barely adequate. Assuming the truth of the vitamin defi-

ciency theory concerning the etiology of beriberi, two explanations suggest themselves: (*a*) the vitamin B requirement of these men was higher than that predicted by our new formula; or (*b*) the red rice used in these experiments happened to be a sample unusually low in vitamin B content. In order to explain the incidence of beriberi in endemic areas among people using undermilled or parboiled (red) rice, Vedder and Feliciano (1928) have suggested that "it seems probable that excessive washing of rice, boiling in an excessive quantity of water, or some other peculiarity in its preparation, is sufficient" to account for this. The same authors cite an instance in the Far East of two neighboring institutions, a monastery and a convent, that had been supplied with the same rice. There was no beriberi in the monastery, but the disease was prevalent in the convent. "We were later informed by Dr. Victor G. Heiser that on investigation it was found that the monks were not very particular about washing their rice, but that the nuns, with true feminine insistence upon cleanliness, washed their rice very thoroughly, and that this simple procedure was the explanation of the peculiar incidence of beriberi among the nuns."[1]

Now soaking in water and steaming are incident to the parboiling process, and it is obvious that details as to amount of water used, time, and other factors, may vary considerably. It is perfectly possible, therefore, that the red rice used in Strong and Crowell's experiments actually was relatively quite low in vitamin B content, at least low enough to make its use in these particular dietaries result in a ration borderline in vitamin B content. This would explain how four of the men in group III escaped beriberi, and two developed the disease. In the absence of any actual tests on animals of the red rice here used, this explanation does not seem to be an untenable one.

The results of the application of our new method for estimation of vitamin B content of foods to the diets used in the Strong and Crowell experiments may be summarized briefly. In all of the cases, where vitamin index values of the foods used are available, and therefore the calculations involve a fair degree of accuracy, the findings agree with the writer's thesis. In those instances where accurate estimates could not be made, two individuals were defi-

1. Vedder and Feliciano, p. 381.

nite exceptions; the results in these cases are opposed to the thesis advanced. Considerations are offered for believing that the findings in these instances can be explained in a manner harmonizing with the thesis. In the absence of certain critical data, the matter must be left in an inconclusive state.

TABLE 34

Beriberi in Relation to the Vitamin B Contents of the Diets Used in the Selangor Gaols, 1892–1902

(Braddon, 1907, pp. 481–511)

YEAR	INCIDENCE OF BERIBERI		VITAMIN B CONTENT OF DAILY RATION					
			Ordinary diet		Penal diet		Alternating ordinary and penal diets	
	Number of cases	Rate per 1,000*	VIT/CAL	Weight for which this is adequate	VIT/CAL	Weight for which this is adequate	VIT/CAL	Weight for which this is adequate
				kgm.		*kgm.*		*kgm.*
1892	10†	57	1.87	66	0.46	16	1.38	49
1893	4	14	2.19	74	1.53	54	1.91	68
1894	4	14						
1895	152‡	200	1.44	51	1.53	54	1.47	52
1896	499§	709						
1897	297¶	767						
1898	73‖	189						
1899	81	207	1.11	39	1.51	53	1.27	45
1900	203	332	0.98	35	0.70	25	0.88	31
1901	216	119	0.91	32	....	..	....	..
1902	901	770	1.12	39	0.68	24	0.97	35

* Braddon, 1907, p. 252.
† Six cases were not contracted in gaol.
‡ One-sixth of these "came into prison with it" (Braddon, p. 487). Forty-eight cases were admitted with beriberi and 33 suffered from relapses, leaving 71 cases developing in gaol.
§ Seventy-eight developed in gaol.
¶ Ninety-seven developed in gaol.
‖ Twenty developed in gaol.

In Public Institutions in Relation to Incidence of Beriberi

Selangor Gaols, 1892 to 1902, Inclusive

In his extensive study of beriberi Braddon (1907) collected data on the rations used in the Selangor Gaols, 1892–1902, and the incidence of the disease during the same period. These diets have been examined with respect to their vitamin B content, and the results checked against the data for the prevalence of beriberi.

During the period under consideration, with the exception of

1901, three ration schemes were followed. All short-term prisoners, whose sentences were under three months, received what was called the *penal diet* daily. Often this ration was practically nothing but rice and salt. All prisoners serving sentences of from three to six months were given the *ordinary diet* four days a week alternating with the penal diet thrice weekly. All long-sentence prisoners, after the first six months of incarceration, received the ordinary diet daily. In the exceptional year, 1901, Dr. H. Wright made experiments which involved placing all prisoners on the same diet. In order to obtain a more complete picture of the probable vitamin intake of the prisoners, the vitamin content of each of these rations has been estimated. Table 34 summarizes the results of these calculations and also presents data on the incidence of beriberi for the periods during which the respective diets were in use.

"In the Selangor prisons the vast majority of the prisoners are only committed for quite short terms, most of them for a few days or a month, a small minority for periods exceeding six months, few for more than a year." (Braddon, p. 495.) Inasmuch as it has been shown by Frazer and Stanton (1909) and by Strong and Crowell (1912) that about three months of subsistence on a polished rice diet are required for the development of beriberi in man, we may devote our attention more particularly to the data for the "ordinary diet" and the "alternating diet" when examining Table 34. Any cases of beriberi appearing among the short-term prisoners who receive the penal diet, would doubtless be individuals whose dietary previous to incarceration had been very low in vitamin.

In 1892 ten cases of beriberi appeared in a daily prison strength of 177 giving a rate of 57 per 1,000. Careful examination of the records by Braddon revealed that 6 of these cases "were not contracted in gaol." Therefore the incidence more representative of the effect of the prison dietary may be expressed as 4 cases with a rate of 23 per 1,000. The ordinary diet for 1892 had a VIT/CAL value of 1.87, which is sufficient for a man weighing about 66 kgm.; the value for the alternating diet that year calculates as 1.38, which would be just adequate for a body weight of 49 kgm. With the men ranging in weight from about 40 to 60 kilos, it is obvious that the dietary in use did not provide any appreciable factor of safety. It is not surprising, therefore, that 4 cases of beriberi appeared.

The same number of cases appeared in 1893, but owing to a great increase in the prison population, the rate per 1,000 was only 14. The rations were much better this year. The ordinary diet had been improved so as to yield a VIT/CAL value as high as 2.19, adequate for a body weight of 74 kilos; and because of the changes made in the penal diet, by which the vitamin content of this ration was approximately trebled, the alternating diet was made sufficient for men weighing 68 kilos, the VIT/CAL value being 1.91. Use of this dietary through 1894 was associated with the same incidence of beriberi as in the previous year.

In 1895 certain changes were made in the rations. In the case of the ordinary diet these consisted chiefly in reducing slightly the amount of rice, and in omitting the fresh fish; the penal diet was altered by substituting bread for wheat flour. As a result of these changes the VIT/CAL ratio of the ordinary diet was reduced to 1.44, adequate for a weight of 51 kilos, which is almost identical with the probable average weight of 52 kilos; the penal ration was actually slightly superior, having a value of 1.53; the alternating diet was intermediate, the VIT/CAL ratio being 1.47. Here, then, we find a dietary just barely sufficient for men of average body weight. There is no factor of safety whatever for men weighing more than the average. It is not surprising, therefore, that use of this dietary for the years 1895, 1896, 1897, and 1898, was associated with the presence of beriberi in epidemic proportions, the number of cases *developing within the prisons* being 71, 78, 97, and 20 for these years, respectively.

In 1899 another change was made in the prison dietary. Dhal was omitted and *towgay*, described by Dr. H. Wright as a "highly nitrogenized germinating bean" was substituted. If we assume that towgay is the same as bean sprouts, then it appears that this change reduced the vitamin content of the ration somewhat. It is interesting, therefore, to see in column 3 of Table 34, that this slight reduction in vitamin was associated with a slight increase in the rate of beriberi incidence.

The alterations made in the ration for 1900 further reduced the amount of vitamin contained in the dietary as will be seen from Table 34. The chief changes consisted in omitting the two most important protective foods, namely beans and dhal, from both the

ordinary and the penal diet. As a result the ordinary ration acquired a VIT/CAL value as low as 0.98, just adequate for a weight of 35 kgm., and the other diets were even lower than this. In 1901 salt fish was omitted from the dietary with a resultant still smaller amount of vitamin. This same year, also, the penal diet was abolished; all prisoners were fed the same ration, but, unfortunately, the diet was markedly deficient in vitamin. Use of these new diets in 1900 and 1901 was associated with a very marked increase in beriberi, the rate being more than doubled. In 1902 the only improvements made in the diet consisted in restoration of salt fish to the ration and a slight increase in the amount of vegetables; during the same year, also, a return was made to the penal diet system. The vitamin content of the ration was increased only very slightly, and this was associated with a severe outbreak of beriberi.

The data for 1902 are the only ones of this group which fail to show the inverse relation of beriberi incidence to vitamin content of the diet. Thus far I have not been able to find in available records any facts by which to explain this exception. It is possible that a greater proportion of the men entered with beriberi; Braddon's data do not indicate how many of the 1901 cases for 1902 developed in the gaol. The district hospital at Kuala Lumpur had a marked increase in the number of beriberi patients during 1902, and this might be taken to mean that the disease was more prevalent outside of the prison that year; against this may be cited the fact that the number of cases for all out-station hospitals in Selangor, did not change appreciably from the previous year, the numbers for 1901 and 1902 being 166 and 160, respectively. It is possible that in 1902 there was some difficulty in securing fresh meat, salt fish, or green vegetables, which with towgay and oil were the chief supplements of the rice. With the diet as prescribed by the prison authorities already definitely low in vitamin, any failure to supply these supplements, or to eat them if supplied, could very easily precipitate a catastrophe. In the absence of available data in the literature one can only speculate as to the cause of the outbreak in 1902.

Inspection of the data in columns 3 and 4 of Table 34 and the plot in Chart 7 reveals in general an inverse relationship existing between the incidence of beriberi and the vitamin B contents of

the "ordinary" diets used in the Selangor Gaols. In preparing the graph the "ordinary" diets were used, rather than the "penal" ration or the combination of these, because these were the dietaries employed in feeding the long-term prisoners. Braddon showed, by careful analysis of statistical data, that the men serving long sentences were many more times liable to beriberi than the short-

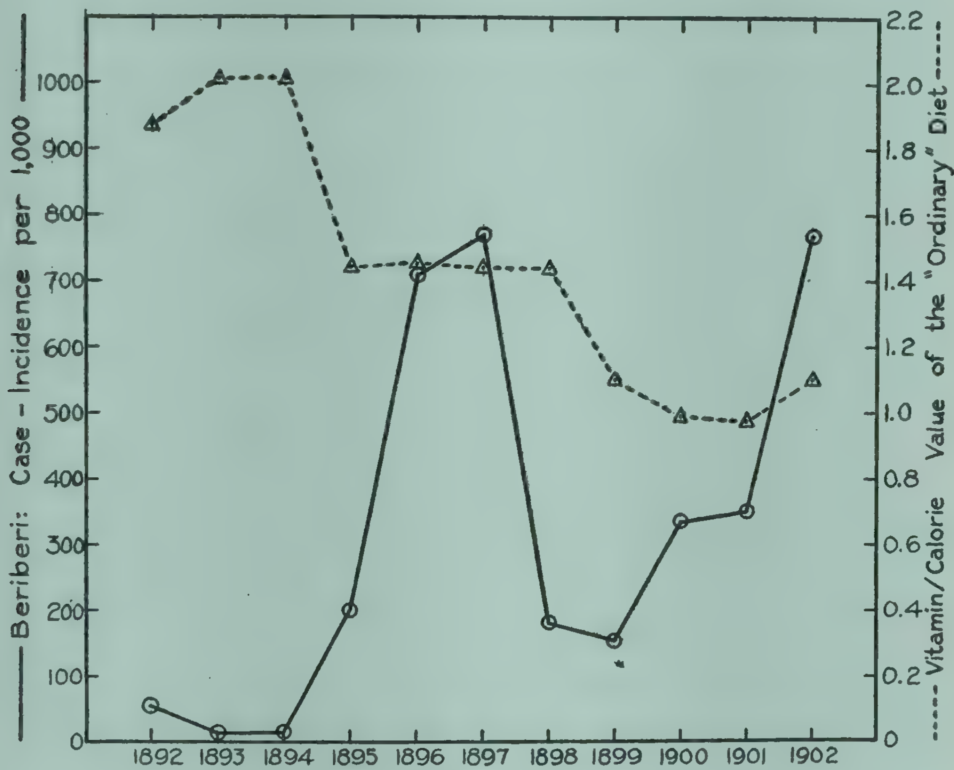

CHART 7

The Relation between Incidence of Beriberi and the Vitamin B (B_1) Content of the Diets Used in the Selangor Gaols, 1892–1902.

term prisoners, a fact which is readily understood in the light of more modern knowledge as to the time required for this disease to develop. The available statistics do not enable us to determine for each of the years in question just how many of the cases of beriberi developed within the prison, and how many were relapses, or represented individuals who entered the gaol with the disease. Therefore, one cannot say, absolutely, that association of a diet

having a VIT/CAL value of 2.19 (see years 1893 and 1894, Chart, 7) with a very slight incidence of beriberi proves that the vitamin B minimum for men weighing from 40 to 60 kilograms is slightly greater than this value of 2.19 represents. Table 34 shows that the values for the "penal" and the "alternating" diets for these same years were definitely lower than this, and many of the men undoubtedly subsisted on these other rations for a considerable period before receiving the "ordinary" diet.

The "ordinary" diet used during the years 1895 to 1898, inclusive, is definitely deficient in vitamin B. This being the case, one should expect a rise in the incidence of beriberi during the period when this ration was used. The fact that the extent of the rise varied somewhat may be taken as indicating that other factors, known to increase the vitamin requirement significantly (see Chapter VIII, p. 65 *et seq.*), were operating but in varying degrees during these years. Therefore these changes in the case-incidence for the period 1895–1898 can hardly be cited as an argument against the definitely inverse relation between the incidence of beriberi and the calculated vitamin B contents of the diets used, which the graph otherwise shows. To the writer, the fact that this inverse relationship is so regular, indicates that the method used to evaluate the diets with respect to vitamin B has real merit. It is difficult to believe that such a regularity could be the result of chance operation of a completely erroneous procedure. Therefore, these data are believed to support the thesis here advanced, that the vitamin B content of human diets can now be estimated with reasonable accuracy, and man's requirement for this dietary factor has been ascertained with a fair degree of approximation.

Singapore Criminal Prison, 1869 to 1901, Inclusive

BRADDON (1907, pp. 501–510) has collected numerous data concerning the rations in force in the Singapore Criminal Prison between 1869 and 1901, as well as the incidence of beriberi during the same period. All of the ten diets described by Braddon have been studied with reference to their vitamin B content. Column 1 of Table 35 is a summary of these findings, tabulated so as to indicate as far as possible the period over which any given dietary was fed. Details of the rations in use during the second half of 1876, the

years 1877 and 1878, and for 1879 up to November, were not available to Braddon, and therefore could not be studied.

During the period 1869 to 1875, there was no definite record of the presence of beriberi in the Singapore Prison. In the Report of a Committee of Inquiry submitted in 1880, however, the medical officer is reported to have said:[1] "Although there is no reliable evidence that beriberi existed in the prison before 1875, yet there is presumptive evidence that this was so, the cases having been recorded under the names of 'general dropsy,' 'chronic rheumatism,' and 'paralysis.'"[2]

The first official record of the presence of beriberi refers to the epidemic which broke out in April, 1875. During the next decade the disease appeared every year, the rate of case-incidence fluctuating appreciably; several changes were made in the prison ration during this period in an attempt to prevent the development of beriberi. In 1885, coincident with another change in the dietary, beriberi totally disappeared from among the prisoners, although, as Braddon pointed out, "continuing with unabated activity among similar classes outside the prison."

> This exemption of the prisoners continued for twelve years, but in 1897 (the proportion of rice in the dietary having again been increased) the disease reappeared, and continued to scourge the prison severely till 1903, in which last year there was a general and simultaneous diminution of the disease in almost every quarter where it had previously prevailed.

Reference to column 1, Table 35 shows that the diet for the first half of 1876 was very slightly superior to that for 1875. This was due to discontinuance of the "penal diet" system which involved feeding only rice and salt ten days of each month. In 1879, this system was reintroduced, with a corresponding lowering of the average daily vitamin intake, and a marked increase in beriberi, which continued to mount greatly during the first half of 1880. As a result of this a Committee of Inquiry was appointed to deal with this 1880 outbreak. In the light of what is now known concerning the cause of beriberi, it is interesting to read in the report of this committee, that "the prisoners had not been overcrowded in any

1. Cited by Braddon, p. 502.
2. *Straits Settlements Government Gazette* (Blue Book, Straits Settlements), 1881.

way. . . . The whole of the prison had been fully repaired, lime-washed, and painted, and fumigations throughout all the dormitories continued to be carried out with regularity." With respect to the ration in use, this committee stated that it was "sufficient in *quantity*."[1] Dr. Rowell, the medical officer, felt "assured that the dietary *per se* cannot be credited with having been a factor in the

TABLE 35

Beriberi and the Vitamin B Contents of Diets Used in Singapore Prison, 1875–1901

(Braddon, 1907, pp. 501–510)

<table>
<tr><th>VITAMIN/CALORIES IN DAILY DIET</th><th>PERIOD</th><th>BERIBERI: CASE-INCIDENCE PER 1,000 OF DAILY AVERAGE STRENGTH OF PRISONERS</th></tr>
<tr><td rowspan="2">0.68</td><td>1869 to 1875</td><td>(Probably always severe—annual mortality 24 per 1,000)</td></tr>
<tr><td>1875</td><td>921</td></tr>
<tr><td>0.81</td><td>1876 (Jan. to July)</td><td rowspan="2">159 or more</td></tr>
<tr><td>?</td><td>1876 (July to Dec.)</td></tr>
<tr><td>?</td><td>1877</td><td>"Slight—a few cases"</td></tr>
<tr><td>?</td><td>1878</td><td>153 or more</td></tr>
<tr><td>?</td><td>1879 (to Nov.)</td><td rowspan="2">388</td></tr>
<tr><td rowspan="2">0.68</td><td>1879 (Nov. to Dec.)</td></tr>
<tr><td>1880 (to July)</td><td rowspan="2">748</td></tr>
<tr><td rowspan="2">1.58</td><td>1880 (July to Dec.)</td></tr>
<tr><td>1881 (to Sept.)</td><td rowspan="2">332</td></tr>
<tr><td rowspan="2">1.86</td><td>1881 (Sept. to Dec.)</td></tr>
<tr><td>1882 (Jan. to Sept.)</td><td rowspan="2">126</td></tr>
<tr><td rowspan="4">1.93</td><td>1882 (Sept. to Dec.)</td></tr>
<tr><td>1883</td><td>28</td></tr>
<tr><td>1884</td><td>10</td></tr>
<tr><td>1885 (to July)</td><td>98</td></tr>
<tr><td rowspan="2">2.24</td><td>1885 (July to Dec.)</td><td>0</td></tr>
<tr><td>1886 to 1896</td><td>0</td></tr>
<tr><td>1.38</td><td>1897</td><td>7 cases (Sept. to Dec.)</td></tr>
<tr><td rowspan="2">1.65</td><td>1898</td><td>154</td></tr>
<tr><td>1899</td><td>213</td></tr>
<tr><td rowspan="2">1.32</td><td>1900</td><td>266·</td></tr>
<tr><td>1901</td><td>252</td></tr>
</table>

causation of the disease. It is a prison diet, but it is one which is liberal, sufficiently nutritious, and varied," etc.

In view of these expressions of confidence in the ration used, it seems surprising that alterations should have been proposed and adopted. Evidently, opinions as to the completely satisfactory

1. Italics are mine.

character of the diet were not unanimous, for definite changes were instituted. In July, 1880, four ounces of rice in the previous dietary were replaced by the same amount of dhal. Reference to Table 35 shows that this increased the vitamin B content of the ration sufficient to give a VIT/CAL value of 1.58. Chart 8 shows that this

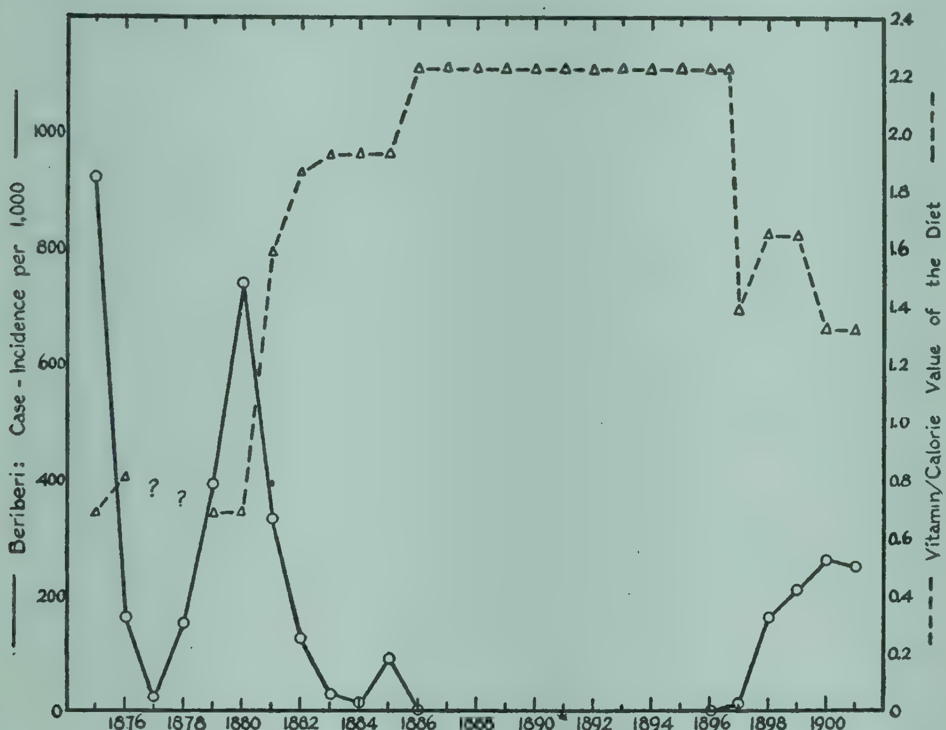

CHART 8

The Relation between Incidence of Beriberi and the Vitamin B (B_1) Content of the Diets Used in the Singapore Criminal Prison, 1875–1901. It will be noticed that when the VIT/CAL value of the ration was approximately 1.9 (years 1883, 1884 and 1885) the incidence of beriberi was very low indicating that this diet furnished very close to the minimum amount of vitamin B (B_1) required by the prisoners. When the VIT/CAL value of the ration was increased to 2.2, and a slight factor of safety against beriberi thus obtained, *beriberi was absent from the prison as long as this diet was used, i.e.* during a period of slightly over 11 years.

change was associated with a marked drop in the incidence of beriberi. This ration was in force until September, 1881, when still further alterations were made resulting in a slight increase in the vitamin content. The most important change made at this time was

the addition of a liberal quantity of beans to the diet. This was followed by about six months of complete freedom from beriberi. Then an outbreak occurred, as in former years beginning in August, the last new case being admitted on October 23rd. "In the epidemics of every previous year the months of November and December had contributed large numbers of cases, and it will be seen that this was a feature also in subsequent years. This abrupt cessation of the 1882 epidemy in October, therefore, seems remarkable. But there is the usual explanation."[1] Changes were made in the dietary which, according to our calculations, increased the vitamin content somewhat. In all probability the amount of vitamin B received by the prisoner was slightly greater than that indicated by our estimations, because Simon, in the Annual Medical Report for 1882, states that "while the outbreak was at its height, a pineapple was given each prisoner daily, on the ground of its having proved useful in Riouw Prison."

This ration continued from September, 1882, to July, 1885, so far as I can determine from Braddon's collection of data. In 1885, there was another outbreak of beriberi; reasons for this epidemic are not evident from the records available. Although this outbreak was not as severe as many of those in previous years, it was serious enough to warrant still further alterations in the dietary. The data in Table 35, and the graph in Chart 8, show that the ration adopted at this time had a sufficient factor of safety to prevent completely the appearance of beriberi. *The disease was absent from the prison for over eleven years.*

For some unknown reason, perhaps the desire to reduce prison costs, in 1895, the quantity of rice in the diet was increased. Such a change naturally reduced the factor of safety against beriberi. I cannot determine, from the data available, just how much rice was introduced, and therefore cannot calculate the extent of the change in vitamin B content produced thereby. No beriberi appeared in the following year—1896—but in 1897, commencing with 7 cases in September, the case-incidence for this disease rose, and continued in 1898, to the proportions of a serious epidemic, which lasted with varying fluctuations down to the spring of 1903.

1. Braddon, 1907, p. 508.

The plot in Chart 8, of the case-incidence of beriberi and the VIT/CAL values of the diets used, shows, in general, the same interesting relationship existing between these variables as was observed in Chart 7 with the Selangor Gaol data. The only exceptions occur in the years 1885, 1898 and 1899. With regard to the data for 1885, it is possible to adopt the view that the diet in use at that time was only barely adequate: the supply of vitamin to be drawn upon to meet a significant increase in the requirement, due to malaria, diarrhea, or other conditions, was too small, or even nil. When the VIT/CAL ratio was increased still more, from 1.93 to 2.24, the factor of safety was increased sufficiently to protect the entire prison against beriberi for as long as the diet was used—over a decade.

These data relating to the Singapore Criminal Prison fail to support the writer's thesis, to the extent that they indicate the daily vitamin need of men weighing from 40 to 60 kgm. to be slightly greater than that predicted by the formula developed for the human species. According to Chart 6 (p. 110), a man weighing 60 kgm. requires daily a diet with a VIT/CAL value of about 1.7; the value 1.93 was almost adequate for the Singapore Prison, but failed definitely in 1885; when the value was increased to 2.24, complete protection against beriberi was obtained.

When one reflects on the facts, that these seemingly high values for the Singapore Prison refer to a locality where diarrhea due to dysentary and other causes is of extremely common occurrence, and this condition conceivably can operate to cause loss of much ingested vitamin, he finds little difficulty in harmonizing these data with the numerous others which have been presented. It also seems significant to the writer that the values of the VIT/CAL ratio just cited and indicative of the vitamin B minimum should be so close to those yielded by the data of Aykroyd for Newfoundland and Labrador families.

Bilibid Prison, Manila, Epidemic of 1901–1902

Late in 1901 there was a change in the ration for the inmates of Bilibid Prison, in Manila, Philippine Islands. This was soon followed by an epidemic of beriberi which reached alarming proportions, there being 1,087 cases during February, 1902, about two

months after the dietary change was instituted. In Table 36 are presented the monthly number of cases and deaths for this period, as reported by Vedder.[1] There were 5,448 cases with 229 deaths, between November, 1901 and January 15, 1903. Beriberi appeared in all parts of the prison simultaneously. "Hospital attendants did not contract the disease, and prisoners who worked in the kitchen seldom were attacked."

On October 20, 1902, after many attempts to combat the epidemic by disinfection of quarters, and similar methods, the ration

TABLE 36

Number of Cases of Beriberi with Deaths in Bilibid Prison, Manila, Philippine Islands, November, 1901 to January 15, 1903

(Vedder, 1913, p. 152)

YEAR	MONTH	CASES	DEATHS
1901	November	2	0
Ration changed			
1901	December	52	2
1902	January	169	12
1902	February	1,087	16
1902	March	576	15
1902	April	327	15
1902	May	310	19
1902	June	451	17
1902	July	233	33
1902	August	571	24
1902	September	522	31
Ration again changed			
1902	October	579	34
1902	November	476	8
1902	December	89	3
1903	January 1–15	4	0
Total		5,448	229

was changed. Inspection of Table 36 shows that following this change of diet there was a *gradual disappearance of beriberi, although the disease did not disappear completely.*

About two years after this epidemic, when the prison contained over 4,000 prisoners instead of 2,000, and was crowded far beyond its capacity, there was no increase of beriberi, although the disease was endemic at the time.[2]

1. Vedder, (1913), p. 152.
2. Quoted from Vedder (1913), pp. 150–151. Italics are mine.

Vedder cites this as evidence against the view that beriberi did not entirely disappear as a result of the change in the ration made October 20, 1902, a fact readily explained by our analysis of this ration with respect to vitamin B content.

The ration in use when the epidemic was at its height has been described in some detail by Vedder and is presented in Table 37 together with an estimation of its vitamin B content. It will be noticed that the ratio of vitamin to calories for this diet has the

TABLE 37

Ration of Convicts at Bilibid Prison, Manila, from December 1, 1901, to October, 1902. During this Period 4,300 Cases of Beriberi Appeared

(Vedder, 1913, p. 151)

COMPONENTS	AMOUNT	VITAMIN INDEX	VITAMIN B CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Bread	151	2	302	391
Rice	454	1.6	726	1,594
Beef	227	5	1,135	454
Potato	85	3.8	323	82
Onions	28	2.7	76	14
Sugar	28	0	0	112
Pepper	0.5	0	0	0
Vinegar	10	0	0	0
Salt	18	0	0	0
Ginger root	28	2	56	14
Total			2,618	2,661
VIT/CAL			0.98	
Body weight for which VIT/CAL value of 0.98 is just adequate			35 kgm.	
Body weights of Philippino men (Aron, 1909)			"About 50–55 kgm."	

value 0.98, which, according to Chart 6, is just adequate for a man weighing 35 kgm. The weight of the male Philippino is recorded by Aron (1909) as "about 50 to 55 kgm." It is quite obvious that a very large proportion of the prisoners in the Bilibid Prison should have developed beriberi while subsisting upon the diet given in Table 37.

The changes made in the ration in use, when the epidemic developed, consisted essentially in reducing the rice component by one-half, doubling the consumption of bread and increasing the

allowances of potatoes and onions. The vitamin B content of the changed diet has been calculated; the results are shown in Table 38 It appears that the new ration contained more vitamin but was still inadequate. The value of the VIT/CAL ratio was raised to 1.29, which, according to Chart 6, just suffices for a man weighing 46 kgm. It is significant that there was a tremendous improvement in the prison with respect to the incidence of beriberi, *but the disease did not disappear entirely.*

TABLE 38

Ration of Convicts at Bilibid Prison, Manila, Introduced in October, 1902. The Incidence of Beriberi was Markedly Reduced After this Date

(Vedder, 1913, p. 151)

COMPONENTS	AMOUNT	VITAMIN INDEX	VITAMIN B CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Bread	302	2	604	782
Rice	255	1.6	408	895
Beef	227	5	1,135	454
Dried fish	57	8	456	200
Potato	119	3.8	452	115
Onions	102	2.7	275	50
Sugar	28	0	0	112
Salt	18	0	0	0
Vinegar	10	0	0	0
Ginger root	28	2	56	14
Pepper	0.5	0	0	0
Total			3,386	2,622
VIT/CAL			1.29	
Body weight for which VIT/CAL value of 1.29 is just adequate			46 kgm.	
Body weights of Philippino men (Aron, 1909)			"About 50–55 kgm."	

It is quite possible that the bread used in the prison was somewhat better from the standpoint of vitamin B content than the bread for which a reasonably accurate vitamin index value is available. If the flour in use in the prison was of cheaper, or of "poorer" quality as judged by modern milling processes, then the bread prepared from it had a higher vitamin content than the index value of 2 would represent. In this case the total vitamin content of the diets shown in Tables 37 and 38 would be somewhat greater than

the amounts indicated. This might perhaps explain why the incidence of beriberi was not greater when the ration shown in Table 38 was used.

It is of interest to compare these rations with that in use in the same prison during 1912, when beriberi was absent. From the diets for each day of the week as described by Strong and Crowell (1912)

TABLE 39

Regular Diet for Native and Asiatic Prisoners in Bilibid Prison, Manila, in Force January to May, 1912

The ration "per day" is estimated from the daily rations as given by Strong and Crowell, 1912, p. 399.

COMPONENT	AMOUNT PER MAN PER DAY	VITAMIN INDEX	VITAMIN CONTENT	CALORIES
	grams		*mgm.-eq.*	
Beef, forequarter	57	5	285	114
Pork, fresh	20	37	740	50
Fish, dried	43	8	344	43
Mongos	97	23	2,231	340
Potatoes	150	3.8	450	125
Camotes	171	3	513	170
Onions	57	2.7	154	28
Rice	400	1.6	640	1,400
Tomatoes	15	2.6	39	3
Bread	166	2	332	430
Sugar	50	0	0	200
Salt	17	0	0	0
Tea	20	0	0	0
Coffee	17	0	0	0
Ginger root	17	3 ?	51	8
Vinegar	6.5	0	0	0
Total per day			5,779	2,911
VIT/CAL			1.97	
Daily vitamin intake if man eats of this ration in sufficient amounts daily to meet his energy requirement			4,100 mgm.-eq.	
Body weight for which this value of VIT/CAL is just adequate			70 kgm.	

and presented in Table 39, the average daily intake of the different foods has been estimated, and from this the amount of vitamin B ingested. The results of these estimations are presented in Table 39. This diet had a VIT/CAL value of 1.97, which is adequate for a man weighing 70 kgm. The ration, therefore, had a slight factor of safety against beriberi.

The application of our methods for estimating vitamin B content to these Bilibid Prison diets leads, then, to the conclusions: (*a*) that the ration, in use when the 1901–1902 epidemic occurred, was markedly deficient in vitamin B and should have allowed such an epidemic; and (*b*) the new diet introduced October 20, 1902, while furnishing much more of the missing vitamin than the former ration, was still somewhat deficient and therefore should have been associated with a slight incidence of beriberi, a conclusion which is in accord with the facts. The diet in use in 1912 had a slight factor of safety against beriberi, and was associated with absence of the disease.

Magelang Military Hospital, Java

THE observations of Vordermann, who studied beriberi in the Java prisons, were of great significance, chiefly because they directed attention to rice as playing some etiologic rôle. In particular did he show that the use of undermilled rice in place of the polished variety greatly reduced the incidence of the disease. Van Dieren regarded these data as indicating that a toxin is present in white rice, a view later championed by Braddon. Vordermann found it difficult to accept the rice-toxin theory because in certain institutions beriberi occurred almost entirely in one group of individuals, although other groups received the same white rice. In the Magelang Military Hospital, for example, some prisoners were working. This group was free from beriberi as long as red rice was used in the dietary; when the rice was changed to the polished variety, beriberi appeared among these men.

> The rice was one and the same quality as the servants of the hospital establishment used, and was cooked in the identical pots in which the rice destined for the staff was cooked. Moreover, the same white rice served for the diet of the local garrison. Now, with this rice for their food, beriberi appears in 10 percent of the convicts, in very few of the soldiers in garrison or hospital. Yet, according to Dr. Van Dieren's theory, this rice must have had poisonous properties.[1]

Van Dieren, and later Braddon, explained these facts as due to the prisoners eating more rice, "if not absolutely, yet in proportion to the rest of their diet than did the soldiers."[2] The diet in use in

1. Braddon, p. 264.
2. Braddon, p. 265.

the Java prisons, together with its estimated vitamin B content, allowing for the different substitutions, is presented in Table 40. From the calculations it appears that this ration may have been adequate for some of the men but not for all. It is not surprising, therefore, that beriberi appeared "in 10 per cent of the convicts." Of course our estimations can be only approximate. They cannot

TABLE 40

The Vitamin B Content of the Diet Used in the Java Prisons and Found to be Associated with Some Beriberi

(Data of Vordermann, cited by Braddon, 1907, p. 265)

DIETARY COMPONENT	AMOUNT DAILY	VITAMIN INDEX	VITAMIN B CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Rice	750	1.6	1,200	2,632
Flesh	(250)			
As beef	200	5	1,000	400
As pork	50	30	1,500	125
or				
Dried fish	120	8	960	120
or				
Dried meat	120	10	1,200	216
Vegetables	150	3	450	69
Spanish pepper	40	2	80	10
Salt	20	0	0	0

TOTALS	VITAMIN B	CALORIES	VIT/CAL
With flesh as beef and pork	3,930	3,211	1.22
With dried fish	2,690	2,831	0.95
With dried meat	2,930	2,927	1.00
With above combinations in succession	3,283	2,990	1.10
Body weight for which this highest value of VIT/CAL is just adequate			43 kgm.
Probable body weight of prisoners			From 40 to 60 kgm.

take account of the variations in food intake due to differences in selections of the foods offered.

With regard to the relatively greater freedom of the local garrison from beriberi, it is pertinent to quote Vordermann, who wrote: "It must be admitted, too, that the rations of the soldiery at Magelang at that time were such that they were enabled with the help of proper adjuncts, to prevent the onset of beriberi."[1] The exact com-

1. Braddon's translation (p. 265) of Vordermann's writing.

position of the ration of the garrison, unfortunately, is not available for study. In view of Vordermann's remark, it is likely that the diet of the soldiers contained less rice, and therefore should have had a slightly greater vitamin B content than the ration presented in Table 40. It would have been almost impossible to secure the same number of calories represented by the difference in rice in the form of any other available foods without obtaining an appreciable amount of the vitamin.

The relative immunity from beriberi of the servants of the hospital is doubtless explained as due to a greater intake of various foods other than rice. Goldberger actually observed in pellagra hospitals a difference between the foods offered to, and consumed by the pellagra patients on the one hand, and the hospital attendants on the other. The servants had greater opportunity to vary their food intake than did the patients.

The findings presented in Table 40 may be summarized as follows: (*a*) the diet for the prisoners at the Magelang Military Hospital was slightly deficient, at least borderline, with respect to adequacy of vitamin B content; and (*b*) this was associated with a moderate incidence of beriberi.

Richmond Asylum, Dublin, 1897

The outbreaks of beriberi which occurred in the Richmond Asylum, Dublin, 1894–1897, have been cited as evidence against the view that this disease is due to poisoning by white rice, because this food was used to only a very limited degree in this institution. The extent to which beriberi occurred at the Richmond Asylum is shown in Table 41.

Considering all of the cases appearing in the four-year period, the average incidence per 1,000 was 106. The larger number of cases occurring among females is worthy of comment, this being contrary to the usual experience. In 1894 the staff of the asylum was not affected; in 1896 seven of the nurses developed beriberi, and in 1897, six nurses and two male attendants contracted the disease.

The only ration available for study in this connection is the one in use during 1897. This diet and the details of the calculations for vitamin B content are shown in Table 42. It appears that this

dietary was borderline with respect to ability to meet the daily vitamin B need; certainly the factor of safety was very small. The value of the VIT/CAL ratio proves to be 1.93, which is considered

TABLE 41

Incidence of Beriberi at the Richmond Asylum, Dublin

(Braddon, 1907, p. 427)

YEAR	DAILY AVERAGE NUMBER OF PATIENTS	CASES OF BERIBERI			RATE PER 1,000
		Male	Female	Total	
1894	1,503	127	47	174	116
1895	?	0	0	0	0
1896	1,686	31	76	107	64
1897	1,800	47	199	246	137
Total......	(av.) 1,663	205	322	527	(av.) 106

TABLE 42

Vitamin B Content of the Dietary in Use at the Richmond Asylum, Dublin, During the Beriberi Epidemic of 1897

(Braddon, 1907, p. 430)

DIETARY COMPONENT	AMOUNT DAILY	VITAMIN INDEX	VITAMIN CONTENT PER WEEK	CALORIES, APPROXIMATELY, PER WEEK
	grams		*mgm.-eq.*	
Bread (daily)..................	680	2	9,520	12,376
Meat:				
Beef (5 days a week)..........	227	5	5,775	2,270
Fish (1 day a week)...........	227	4.5	1,022	227
Bacon (1 day a week).........	227	18	4,086	1,419
Potatoes (daily)................	454	3.8	12,075	3,080
Vegetables (daily)..............	454	3	9,534	1,589
Totals:				
Per week....................................			42,012	20,961
Per day......................................			6,002	2,994
VIT/CAL......................................			1.93	
Body weight for which this value of VIT/CAL is just adequate....................................			68 kgm.	
Probable average body weight of inmates.............			66 kgm.	

to be just adequate for a man weighing 68 kgm. If the *average* man is regarded as weighing 66 kgm., then the ration must have been inadequate for some of the inmates, but not for all. To this extent,

therefore, these results support the thesis being advanced. When, however, one considers the relatively high incidence of 106 cases of beriberi per 1,000 inmates in relation to the estimated vitamin content of the ration and the predicted human requirement for the vitamin, it appears that the calculation indicates the diet to have been better than it really was. This need not be regarded as complete failure of our method. The calculation does indicate the diet to have been adequate only for men weighing less than the average; and when a ration is definitely borderline, it is clear that special predisposing factors other than the diet exert a greater influence in precipitating the disease. Whether an unusually greater incidence of beriberi occurs under these circumstances will depend upon what these other special factors are, and how effective they may be.

In view of these considerations one appears justified in concluding that our method developed for evaluating human diets with respect to vitamin B content is moderately successful, when applied to the data of the 1897 beriberi epidemic at the Richmond Asylum; the accuracy in this instance is less than might be desired.

CHAPTER XII

VITAMIN B CONTENT OF DIETS IN RELATION TO BERIBERI IN MILITARY AND NAVAL ORGANIZATIONS AND OTHER GROUPS

Dutch East Indian Navy, 1870–1880

IN TABLE 43 is shown the incidence of beriberi in the Dutch East Indian Navy for the years 1870–1880, inclusive. Among the native sailors it is evident that the disease occurred continually in epidemic proportions. The European sailors were almost, but not absolutely, free from beriberi. The studies of Van Leent (1880) made it quite clear that this condition was in some way related to the different dietaries in force in the two groups of sailors, and stated the compositions of these rations in more or less detail.

It will be noticed in Table 43 that the incidence among the natives was very high up to 1874 during which year there was a remarkable decrease. During these years—1870 to 1873, inclusive—the diet of the natives was that presented in Table 44. The ration of the European sailors was that given in Table 45. Let us consider these diets with respect to their contents of vitamin B. The details of the calculations of vitamin contents of this ration are given in Table 44.

In making these estimations it is necessary, because of insufficient data, to make certain assumptions with respect to the kind of meat used. Beef and pork are commonly eaten by Malays. It has been assumed, therefore, that the 300 grams of flesh consisted of 225 grams of beef and only 75 grams of pork. Van Leent (1880) stated that the flesh was nearly always lean, yielding at times but little fat, and often none at all (Braddon, 1907, p. 241). One might interpret this to mean that very little pork was really used, and when it was available, it was of the lean variety. In view of this I have taken a high index value for pork, that which applies to lean pork muscle. Even with these assumptions the estimations indicate

that the vitamin B content of the ration was definitely below the minimum. The diet as reported by Braddon lists certain substitutes as allowable. Calculations have been made in an endeavor to

TABLE 43

Incidence of Beriberi in the Dutch East Indian Navy

(Braddon, 1907, p. 241)

YEAR	NATIONALITY OF SAILORS	STRENGTH	CASES OF BERIBERI	PROPORTION OF BERIBERI PER 1,000 OF STRENGTH
1870	Europeans	2,259	14	4.7
	Natives	967	194	206.2
1871	Europeans	2,483	6	2.4
	Natives	831	206	247.0
1872	Europeans	2,326	19	8.1
	Natives	770	199	260.0
1873	Europeans	2,744	24	8.8
	Natives	762	460	603.7
1874	Europeans	2,810	2	0.7
	Natives	722	51	70.6
1875	Europeans	2,934	9	3.6
	Natives	903	129	142.8
1876	Europeans	2,786	1	0.4
	Natives	983	165	168.0
1877	Europeans	2,500	7	2.8
	Natives	1,100	123	111.9
1878	Europeans	About 3,000	0	0.0
	Natives	1,000	54	54.0
1879	Europeans	3,000	0	0.0
	Natives	1,000	23	23.0
1880	21 ships with natives on European diet	1,222	39	31.9
	9 ships with natives on native diet	307	56	182.4

take account of these; the effect of eating the different combinations in succession daily has also been estimated. As shown in Table 45, the description of the diet states that there were also supplements of dried onions and greens. It has been necessary to guess

as to how much of these foods were taken. The question marks in the table are intended to express this fact.

According to Chart 6 the value of the VIT/CAL ratio (Table 45) is just sufficient for a body weight of 73 kgm., which is somewhat greater than the probable average weight of the European sailors. The average weight of 868,445 accepted recruits in the United States Army during 1917 is 64.3 kgm., or 141.5 pounds, (Davenport and Love, 1921). As was pointed out in discussing the

TABLE 44

Dietary of Native Sailors of the Dutch East Indian Navy Prior to 1874

(Braddon, 1907, p. 240)

FOOD	AMOUNT DAILY	VITAMIN INDEX	VITAMIN CONTENT	CALORIES, APPROXIMATELY	VIT/CAL
	grams		*mgm.-eq.*		
Rice	1,000	1.6	1,600	3,510	
Flesh taken as	(300)				
Beef	225	5	1,225	450	
Pork	75	35	2,625	248	
or					
Fish, fresh	300	4.5	1,350	300	
or					
Fish, dried	300	8	2,400	450	
Salt, vinegar, coffee, etc.	.....	....	.....	.....	
Totals:					
With flesh			5,450	4,208	1.30
With fresh fish			2,950	3,810	0.77
With dried fish			4,000	3,960	1.01
With these in succession daily			4,133	3,993	1.04
Body weight for which the highest value of VIT/CAL is just adequate				46 kgm.	
Body weight for which the "in-succession" value for VIT/CAL is just adequate				37 kgm.	
Probable range of body weights of native sailors				40–60 kgm.	

Aykroyd data (see p. 111), the average weight of the recruits of English origin is 66 kgm., a slightly greater figure than that taken in Table 45. In the absence of more accurate data as to the body weights of these sailors, the above figures have been taken as a basis for determining whether the diet was adequate. The calculations as made and recorded in Table 45 indicate a diet that is satisfactory, but with a very low factor of safety; for men weighing over 160 pounds, or 73 kgm., this ration is definitely inadequate.

It is obvious, that unless the supply of pork and beans was appreciably greater than that stated in Table 45, the diet would not be satisfactory for all individuals. The fact that there was a small incidence of beriberi (see Table 43) among the European sailors subsisting on this ration supports the conclusion indicated by the calculation, that this diet was borderline with respect to its adequate supply of vitamin B. Any appreciable variations from the ration as offered, by the special selection of certain of the foods and continued avoidance of others, favored the development of beriberi.

TABLE 45

Dietary of European Sailors in the Dutch East Indian Navy Prior to 1874

(Braddon, 1907, p. 241)

FOOD	AMOUNT DAILY	VITAMIN INDEX	VITAMIN CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Bread	400	2	800	1,040
Rice	500	1.6	800	1,750
Flesh	(400)			
Taken as beef	325	5	1,625	650
Taken as pork	75	35	2,625	248
Lard	75	11	825	675
Butter	35	8	280	263
Beans or grey peas and potatoes	(300)			
Taken as beans	75	23	1,725	263
Taken as potato	225	3.8	855	180
Onions, dried	28?	12	336	100
Greens	57?	10	570	20
and				
Coffee, tea, salt, etc.		0	0	0
Total			10,441	5,189
VIT/CAL			2.05	
Body weight for which this value of VIT/CAL is just adequate (see Chart 6)			73 kgm.	
Probable average body weight of European sailors			About 64 kgm.	

Decreased Incidence of Beriberi Among Native Sailors in 1874 Due to Giving Them the Ration of European Sailors

In order to make clear the factor responsible for the marked decrease in beriberi among the native sailors, which took place in

1874, I cannot do better than to quote Braddon (1907, p. 241 *et seq.*) who had access to the account given by Van Leent (1880).

During the years 1870, 1871, and 1872, while the ships lay off Banka and Borneo, beriberi was very rife among the natives, while among the Europeans but few cases occurred. In 1874, when the vessels were at Atjeh, nearly two-thirds of the natives became attacked, and there was a trifling increase also among the Europeans. Since no other measures served to check this appalling rate of sickness among the natives, "as a last despairing regulation," says Van Leent, "it was ordered that native sailors should be no longer employed in Atjeh waters. They were replaced by Europeans, one for every two natives. This radical and, of course, complete remedy was, however, disapproved by the Dutch Home Government, who feared the danger of thus overworking their own sailors, and on their urgent order, Javanese sailors were once more sent to Atjeh.

"Meanwhile the native *stokers* on the latter ships had been drawing European crews' rations—a regulation which cannot be too much commended—and these were also extended to the Javanese sailors as they rejoined their ships. . . . Never had any sanitary measure a success so complete as this. *Immediately the number of beriberi cases fell very greatly.*"

Increased Incidence of Beriberi Among Native Sailors in 1875, 1876, and 1877 Due to Reversion to Old Native Diet

In Table 43 it will be noticed that among the native sailors beriberi increased again in 1875, 1876 and 1877. The explanation made by Van Leent, and cited by Braddon, is that these occurred chiefly on several ships, which were detached from the Atjeh squadron for work elsewhere—to New Guinea and the Celebes—and which reverted to the old ration for the native sailors. As a result beriberi again increased on these ships. This occurred concomittantly with a continued very low incidence of beriberi at Atjeh where the improved diet was being used, and regarding which Van Leent stated: "The issue of European crews' sea-rations daily to the natives had rooted out the sickness as by magic." Van Leent investigated the cases which continued to appear on a few ships, and found that these were sailors who had not drawn the optional European ration, but preferred the native diet. "Therefore European diet was made compulsory. From that moment beriberi vanished, or almost vanished, on board these ships."

Consideration of the smaller average weights of the native sailors as compared with the Europeans (see tables 44 and 45), and the relation of the VIT/CAL ratio to body weight shown in Chart 6

(p. 110), indicates very clearly that the diet of the European sailors, while inadequate for the heaviest men, offered a slight factor of safety against beriberi when fed to the smaller natives.

New Ration for Native Sailors Introduced January 1, 1878

THE foregoing observations naturally led to attempts to improve the ration offered the native sailors. These efforts culminated in the introduction of a new diet on January 1, 1878. Inspection of Table

TABLE 46

Dietary for Native Sailors in the Dutch East Indian Navy Introduced in 1878

(Braddon, 1907, p. 243)

FOOD	AMOUNT DAILY	VITAMIN INDEX	VITAMIN CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Rice	1,000	1.6	1,600	3,510
Bread	200	2	400	518
Meat	(400)			
Taken as beef	300	5	1,500	600
Taken as pork	100	35	3,500	250
Dried fish	100	8	800	162
Butter and cocoanut oil	(45)			
Taken as butter	22	8	176	167
Taken as cocoanut oil	23	8 ?	184	207
Onions, dried	28 ?	12	336	100
Greens	57 ?	10	570	20
and				
Coffee, tea, salt, etc.		0	0	0
Totals			9,066	5,534
VIT/CAL			1.64	
Body weight for which this value of VIT/CAL is just adequate (see Chart 6)			58 kgm.	
Probable range of body weight of native sailors			40–60 kgm.	

43 shows that following the use of this new ration, the beriberi rate among the native sailors fell to 54 and 23 per 1,000 during 1878 and 1879 respectively.

Details of the new ration, together with an estimation of its vitamin B content, are presented in Table 46. As with the previous diets of these sailors, it has been necessary to make certain assumptions concerning the kinds of meat used, etc., in order to complete the calculation of vitamin content.

Comparison of the results in Table 46 with our estimated daily vitamin B requirement of men having an average body weight approximating that of these native sailors indicates that this new ration classifies as very slightly deficient or borderline with respect to vitamin B content. The probable range of weight for the natives is from 40 to 60 kgm.; the value of the VIT/CAL ratio indicates that the ration just suffices for a man weighing 58 kgm. In other words, heavier men, or men afflicted with malaria, diarrhea, or other disease affecting the vitamin requirement, or individuals who failed to eat the diet precisely as offered, choosing special foods, or avoiding others, any of these individuals was especially liable to beriberi.

This agrees with the observation that, although the incidence of beriberi among the native sailors became much less than formerly, the disease did not entirely disappear. "So far from the cases altogether ceasing, even during the best years, at least 20 to 30 per 1,000 native strength continued to be annually affected" (Braddon, 1907, p. 244).

When it is realized that the adequacy of these rations is being judged by the way calculations based on the index values in Table 21 agree with the human requirements for vitamin B as predicted by our formula, and the results of these estimations check so well with the facts concerning the incidence of beriberi in the Dutch East Indian Fleet, it is difficult to avoid the conclusion that these calculations, approximate as they are, do have real merit.

Japanese Navy, Takaki's Experiments, 1883 and 1884

The experiments of Takaki (1906) showed that the remarkably high incidence of beriberi in the Japanese navy could be prevented by certain changes in the ration of the sailors. Some idea of the importance of this work may be gained from an inspection of the statistics presented in Table 47. It will be noticed that between the years 1878 and 1883 the average case-incidence per annum for the entire navy was *32.45 percent.* In other words, one sailor out of every three, suffered from the disease. It hardly seems necessary to review in detail all of the numerous observations relating to beriberi which Takaki made. They have been described by Braddon (1907) and Vedder (1913). The dietary experiments conducted on

two training ships, however, afford sufficient data for such a study as we have made with many other rations, and will now be considered.

Between December 19, 1882, and September 15, 1883, the training ship Ryujo was on an extensive cruise in Pacific waters. The ship carried 309 marines, 27 cadets and 27 officers and sub-officers,

TABLE 47

*Prevalence of Kakke (beriberi) in the Japanese Navy**

YEAR		AVERAGE STRENGTH OF FORCE	CASES OF KAKKE	PERCENTAGE OF FORCE AFFECTED
Old diet	1878	4,528	1,485	32.8
	1879	5,081	1,978	38.9
	1880	4,956	1,725	34.8
	1881	4,641	1,163	25.0
	1882	4,769	1,929	40.4
	1883	5,346	1,236	23.1
Average		4,887	1,586	32.45
New diet	1884†	5,638	718	12.74
	1885	6,918	41	0.59
	1886	8,475	3	0.04
	1887	9,106	.....	.....
	1888	9,184	.....	.....
	1889	8,954	3	0.03
	1890	9,112	4	0.04
	1891	10,223	1	0.01
	1892	9,747	3	0.03
	1893	9,323	1	0.01
	1894	11,003	29	0.26
	1895	13,006	17	0.13
	1896	13,035	11‡	0.08
	1897	14,964	22	0.14
	1898	18,426	16	0.08
Average		11,018	10	0.07

* From Saneyoshi, cited by Braddon (1907), p. 229.

† New diet introduced. The change ordered, but not brought generally into effect until later in the year.

‡ Years during and after the war with China. There was a scarcity of barley and other exigencies which led to use of large amounts of rice.

and during the cruise of 272 days traveled from Japan to New Zealand, Valparaiso, Honolulu, and then to home ports. During the trip 173 cases of beriberi appeared.[1] The unusually high inci-

1. The accounts given by Braddon and Vedder evidently were taken from Takaki's report. The number of cases, number of men on board, and other items do not agree completely with the data reported by Oshima which are presented in

dence of beriberi on this ship led Takaki to ask for an investigation. A committee studied various phases of the problem including housing, weather and climate, clothing, bedding, amount of labor, food and drink. The proportion of nitrogen to carbon in the ration was emphasized by Takaki as indicating an unfavorable diet. In the light of modern knowledge with respect to vitamin B it is clear that the dietary must have been markedly deficient in this important factor.

Oshima (1905) has collected data concerning the average daily intake per man of various foods used on the cruise of the Ryujo. These are presented in Table 48, together with the results of estimations of the amount of vitamin yielded per day. The chief sources of error in these calculations probably involve the bread used, miso, a soy bean product, and shoyu, or soy sauce. Assays of these materials for vitamin B have not been found by the writer. The vitamin index values indicated in column 2 of Table 48 were selected after considering Oshima's detailed description of these foods. A commercial soy sauce has been assayed by the writer and the results of these tests support the conclusion that a fair index to use for shoyu is 8.

From Table 48 it appears that the food mixture actually eaten by the marines was markedly deficient in vitamin B, the VIT/CAL ratio being only 1.20, a value just adequate for a man weighing 42 kgm., whereas the average weight of Japanese sailors, according to Takaki (1906), was 56 kilos. The vitamin intake of the cadets was somewhat greater as indicated by a VIT/CAL value of 1.41. Similarly, there is improvement in the rations of the sub-officers and officers, the values for these groups being 1.53 and 1.67, respectively. From our formula it is estimated that the diet of men weighing 56 kgm. should have a VIT/CAL value of at least 1.58. These results, approximate as they are, certainly harmonize with the facts concerning the incidence of beriberi in the respective groups. Even the best diet of the series affords so slight a factor of safety that it is not surprising to find that some beriberi was asso-

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Table 47. Braddon states that all of the cases reported by Takaki appeared before the ship touched Honolulu. It is possible that Oshima's tables include other cases which developed later. I have not been able to explain satisfactorily the slight discrepancies in the two reports.

TABLE 48

Vitamin B Contents of the Diets Used on the Japanese Training Ship Ryujo Between December 19, 1882, and September 15, 1883

While on this cruise beriberi appeared. The data on food intake are taken from Oshima, 1905, p. 56 *et seq.*

KIND OF FOOD	VITAMIN INDEX	MARINES		CADETS		SUB-OFFICERS		OFFICERS	
		Amount of food	Vitamin content	Amount of food	Vitamin content	Amount of food	Vitamin content	Amount of food	Vitamin content
		grams	*mgm.-eq.*	*grams*	*mgm.-eq.*	*grams*	*mgm.-eq.*	*grams*	*mgm.-eq.*
Meats	5	94	470	158	790	206	1,030	275	1,375
Fish	4.5	53	239	60	270	83	374	121	545
Eggs	5.5	4	22	12	66	10	55	24	132
Milk	3.6	19	68	57	205	44	158	24	86
Bread	2	81	162	89	178	221	442	145	290
Rice	1.6	612	979	542	867	398	637	501	802
Sugar	0	35	0	74	0	39	0	64	0
Legumes	23	19	437	25	575	11	253	27	621
Miso	3	21	63	19	57	18	54	16	48
Shoyu	8	58	434	51	408	38	304	54	432
Vegetables	3	193	579	307	921	357	1,071	515	1,545
Fats	8	0	0	14	112	23	184	36	288
Totals:									
Vitamin		3,453		4,449		4,562		6,164	
Calories		2,875		3,072		2,867		3,508	
Ratio: Vitamin/Calories		1.20		1.45		1.59		1.76	
Body weight for which this value of VIT/CAL is just adequate		42 kgm.		51 kgm.		56 kgm.		62 kgm.	
Incidence of beriberi:									
Total number of men		309		27		27		?	
Cases of beriberi		164		4		5 "officers and sub-officers" (not distinguished)			
Average body weight of Japanese sailors				56 kgm.					

ciated with its use. As already pointed out, the absolute values expressing the vitamin B contents of these dietaries in all probability are only approximate; subsequent research on the relative vitamin B contents of Japanese foods will doubtless show that the

totals given in Table 48 are in error; it is not likely, however, that the relative vitamin B contents of these rations will be changed appreciably; for this to occur it would be necessary to attribute to the doubtful foods extremely different index values, especially for the bread, of which the officers and sub-officers ate much larger quantities than did the marines and cadets.

Against considerable opposition Takaki succeeded in having the ship Chikuba ordered in 1884 to make the same cruise as the Ryujo

TABLE 49

The Vitamin B Content of the Japanese Navy Ration Provided in Accordance with the Navy Food Supply Act of 1884

Data secured from Oshima, 1905, p. 59

FOOD	AMOUNT DAILY	VITAMIN INDEX	VITAMIN B CONTENT
	grams		*mgm.-eq.*
Meat	300	5	1,500
Fish	150	4.5	675
Milk	45	3.6	162
Fat	15	8	120
Rice	675	1.6	1,080
Or equivalent in Bread	675	2	(1,350)
Sugar	75	0	0
Legumes	45	23	1,035
Miso	52	3	156
Shoyu	60	8	480
Vegetables	450	3	1,350
Condiments, etc.	?	0	0
Total:			
With rice			6,558 } av. 6,693
With bread			6,828 }
Total Calories			4,295
$\frac{\text{Vitamin}}{\text{Calories}}$ = 1.53 and 1.59			av. 1.56

had made previously. The crew of this boat was given the new Japanese Navy Ration provided in accordance with the Navy Food Supply Act of 1884. The Chikuba left Japan on February 3, 1884, and returned on November 14th of the same year after an absence of 287 days. On board the battle ship were 35 officers, 25 naval cadets, and 297 marines. "The number of kakke (beriberi) patients during the voyage was 14, namely 2 cadets and 12 marines. The results were considered most satisfactory." (Oshima, 1905, p. 59).

According to Takaki, "it appears that the cadets (those who developed beriberi) were unable to take condensed milk, of which their fellows took 1 pound weekly; also 8 of the 10 men had been unable to eat meat as the others did."

Table 49 presents an analysis of the new Japanese navy ration provided by the law of 1884. The VIT/CAL value, allowing the substitution of bread for rice, ranged from 1.53 to 1.59, making this new diet about the same in vitamin content as the dietary provided the officers and sub-officers of the Ryujo, on which so much beriberi had occurred among the marines and cadets in 1882 (see Table 48) and to a lesser extent among the officers. The facts (*a*) that the VIT/CAL value of the new ration is so close to the predicted minimum for these sailors, and (*b*) that use of this diet was associated with the development of a few cases of beriberi, seem specially significant and worthy of citation in support of the author's thesis.

Boer War Prisoners at St. Helena, 1901–1902

For a description of the epidemic of beriberi, which occurred among the Boer prisoners on the island of St. Helena, I am indebted to Braddon (1907, p. 436) who had access to the account written by Casey (1903). This epidemic was of particular interest to Braddon because, according to his theory, beriberi is due to rice-intoxication, and rice was not used in the dietary in force in the prisoner's camp at St. Helena. It is interesting, therefore, to find Braddon questioning the diagnosis of beriberi in these cases, although, as Casey pointed out, his diagnosis "was confirmed by Colonel Williamson, P.M.O., when he paid his official visit to St. Helena. He pronounced the cases genuine beriberi." Casey further stated: "it may be mentioned, *en passant*, that the circumstances of the sufferers being Boer prisoners put the question of alcoholic neuritis out of the question."

The dietary in use at the St. Helena prison camp, together with an estimation of its vitamin B content, is given in Table 50. In calculating the vitamin contributions made by the preserved meat and vegetables an index as high as 10 has been used; it is quite likely that this is too high. Even with these high index values the total ration proves to be deficient in vitamin B for some of the men at least. The value of the VIT/CAL ratio certainly could not have

been greater than 1.75, which is just sufficient, according to our prediction formula, for a man weighing 62 kgm.; the average body weight of these prisoners was probably about 66 kgm., which is the figure obtained by Davenport and Love (1921) as the average body weight of the 1918 recruits of the United States Army. The fact, that the rate of incidence of beriberi was as low as 26 per 1,000, correlates very well with our finding that the diet was borderline with respect to its content of vitamin B.

TABLE 50

The Vitamin B Content of the Diet of the Prisoners of War at St. Helena During the Slight Epidemic of Beriberi, 1901–1902

(Braddon, 1907, p. 439)

DIETARY COMPONENT	AMOUNT DAILY	VITAMIN INDEX	VITAMIN CONTENT PER WEEK	CALORIES, APPROXIMATELY PER WEEK
	grams		*mgm.-eq.*	
Bread (6 days a week)	567	2	6,804	8,844
Biscuit (1 day a week)	454	2	908	1,131
Meat, fresh (6 days a week)	454	5	13,620	5,448
Meat, preserved (1 day a week)	340	10 ?	3,400	1,020
Condensed milk, about	70	3.6	1,764	686
Potatoes (6 days a week)	227	3.8	5,178	1,092
or				
Vegetables, preserved mixed (1 day)	28	10 ?	280	28
Totals:				
Per week			31,954	18,249
Per day			4,565	2,607
VIT/CAL			1.75	
Body weight for which this value of VIT/CAL is just adequate			62 kgm.	
Probable body weight of the prisoners, average			66 kgm.	
Incidence of beriberi associated with use of this diet:				
Number of prisoners				3,500
Cases of beriberi				91
Beriberi rate per 1,000				26

Braddon cites Morse, (1904) as stating that many of the prisoners were profoundly depressed. This fact might well be taken as indicating failure of many of the men to eat the diet essentially as furnished; for prisoners restricted to this ration to confine their

selections of foods to some of the dietary components, avoiding others, there could be only one result, namely, the development of beriberi.

British Native Troops in India, 1896–1901

From time to time beriberi has appeared among the British Indian Native Troops but almost entirely, as Braddon (1907, p. 267) has pointed out, among the Madras regiments, who use rice as the staple food instead of attah, which is essentially a whole wheat flour.

> It is in this habit—this addiction to rice—that the Madras troops, the sole sufferers from beriberi in the Indian army, differ from all the other arms—the Bengal Lancers, Infantry and Sappers (including the Rajput regiments), the Goorkhas, the Punjab frontier forces (Panjabis, Sikhs, Dogras, Afridis, and Pathans), and the Bombay army of Mahrattas, Jats, and other Sikhs, Rajputs, and Baluchis—for these latter races who do not get beriberi are almost all eaters of other sorts of grain than rice—wheat, millet, pulses, and corn; while the few who do eat rice—the Bombay Mohammedans, Deccani Mahrattas—use cured[1] grain. . . . The native may draw either attah or rice, but by the Madrasi rice is always preferred. Provisions are at all camps bought locally in the bazar of the station where the troops are quartered. Hence the rice used is always the same as that consumed, and often grown by, the villagers of the neighborhood; and in the case of most of the districts—in the Madras Presidency, at least—this is as much as to say that it is a rice made dry from padi not previously boiled—is, therefore, "uncured", and more or less old and stale, according to circumstances.

In Table 51 are given data concerning the incidence of beriberi in the Madras Command from 1896 to 1901 inclusive.

Fairly detailed information concerning the diets used by these different groups of Indian Troops is available only for the 1899 epidemic in the 2nd Madras Infantry at Vizianagram, and for the detachment of the 9th Infantry at Trincomalee in 1900–1901. The vitamin contents of these rations have been calculated. The results of these estimations will now be presented.

In Table 52 is shown the daily ration of the Indian native troops in use during the period covered by Table 51. According to Braddon this diet is "substantially the same everywhere and for all arms."

1. Also called parboiled rice.

In view of Braddon's statement that "the rice used is always the same as that consumed, and often grown by, the villagers of the neighborhood," there is some uncertainty as to whether the index

TABLE 51

Incidence of Beriberi among Madras Native Troops, from 1896 to 1901 Inclusive

(Braddon, 1907, p. 267)

STATION	YEAR	REGIMENT	NUMBER OF CASES
Vizianagram: 1	1896	20th Madras Infantry	55
" 2	1897		
" 3	1898	2nd " "	73
" 4	1899	" " "	113
" 5	1900	(?) " "	11
" 6	1901	(?) " "	15
Rangoon: 7	1899	7th " "	36
" 8	1900	" " "	12
" 9	1901	8th " "	15
Trincomalee: 10	1900	9th " " detachment of 138 men	9
" 11	1901		36

TABLE 52

Vitamin B Content of the Daily Ration of British Indian Native Troops

(Braddon, 1907, p. 267)

DIETARY COMPONENT	AMOUNT DAILY	VITAMIN INDEX	VITAMIN B CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Attah	906	23	20,838	3,370
or				
Rice (with Madras troops only)	906	1.6	1,450	3,180
Meat (mutton or fowl)	142	5	710	284
Dhal (pulse husked or split)	71	23	1,633	248
Fresh vegetables	170	3	510	85
Onions	14	2.7	38	7
Adjuncts (salt, etc.)	160	0	0	0

	WITH ATTAH	WITH RICE
Total vitamin	23,729	4,341
Total calories	3,994	3,804
VIT/CAL ratio	5.94	1.14
Body weight for which VIT/CAL is adequate	All weights	40 kgm.

value of 1.6 is the correct one to use in the calculations of the vitamin content of these diets. The result of the estimations may therefore be regarded as a minimum; the amount of vitamin present may be greater depending upon the particular kind of rice available.

According to Table 52, the diet containing attah, has a very large amount of vitamin, and use of it, therefore, should not be associated with beriberi. This agrees with the facts. Where rice is used, the value of the VIT/CAL ratio may be as low as 1.14, which is just sufficient for a man weighing about 40 kgm. Inasmuch as the average weight of the Indian soldier is about 56 kilos, it is evident that beriberi may occur among the rice-eating Madrasi; the factor of safety here is represented almost entirely by the quality of the rice being used. If a "cured," or parboiled rice is consumed, no beriberi should occur; if highly polished white rice should be used for an appreciable period, the disease would develop.

In all probability the use of an inferior rice accounts in large measure for the epidemic which occurred at Vizianagram in 1898–1899 (see Table 51). Most of the cases appeared between July and October, 1898 and 1899. All of the men ate large quantities of rice and only small amounts of meat. When the ration shown in Table 53 was employed for the recruits, *i.e.*, men under three years service, there was a tremendous improvement. In the next two years very few cases appeared at Vizianagram. According to calculations the new diet was adequate with respect to vitamin B.

The men at Vizianagram, who developed beriberi in 1898–1899, are recorded as eating only small quantities of the meat component of the ration. It is obviously impossible to estimate accurately the vitamin intake of individuals with unusual food habits; in such cases some knowledge as to what foods are actually eaten is necessary. Another instance where beriberi appeared in individuals, who ate rice but only small quantities of the meat available, is the 1918 epidemic occurring in the garrison of United States troops at San Juan, Porto Rico (see p. 173).

The rations in use at Trincomalee, during and immediately after the epidemic of 1900–1901, are presented in Table 54. If the rice was of the highly polished variety with a vitamin index value as low as 1.6, then the VIT/CAL ratio reached the low value of 0.88, which should be associated with beriberi. If it be assumed that the index for this rice should be 5, the ratio of vitamin to calories is raised to 1.67, which is just adequate for a body weight of 59 kgm. From this it is quite obvious that the factor of safety in the case of

TABLE 53

The Vitamin B Content of the Improved Diet, Use of Which Resulted in Complete Disappearance of the Beriberi Epidemic Among the British Indian Native Troops at Vizianagram in 1899

(Braddon, 1907, p. 269)

DIETARY COMPONENT	AMOUNT PER WEEK	VITAMIN INDEX	VITAMIN B CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Rice, boiled (5 days a week)	4,530	10	45,300	15,900
Attah (2 days a week)	1,812	23	41,676	6,741
Meat, mutton (6 days a week)	1,456	5	7,280	2,912
Dhal (daily)	497	23	11,431	1,764
Potatoes (2 days a week)	272	3.8	1,034	264
Onions (daily)	98	2.7	265	48
Fresh vegetables (5 days a week)	850	3?	2,550	425
Fowl (1 day a week)	113	5	565	124
Total per week			110,101	28,178
Total per day			15,728	4,025
VIT/CAL ratio			3.90	
Body weight for which this value of VIT/CAL is adequate			All weights	
Average body weight of Indian soldier			56 kgm.	

TABLE 54

The Vitamin B Content of the Diets Used by the British Indian Native Troops at Trincomalee Before and After the Beriberi Epidemic of 1900–1901

(Braddon, 1907, p. 270)

FOOD	VITAMIN INDEX	RATION IN USE DURING THE BERIBERI EPIDEMIC OF 1900–1901			RATION INTRODUCED IN 1901 AND ASSOCIATED WITH DISAPPEARANCE OF THE EPIDEMIC		
		Amount daily	Vitamin B content	Calories, approximately	Amount daily	Vitamin B content	Calories, approximately
		grams	*mgm.-eq.*		*grams*	*mgm.-eq.*	
Rice	1.6	906	1,450	3,180	453	725	1,590
Attah	23	0	0	0	453	10,419	1,608
Dhal	23	87	2,001	309	57	1,311	202
Ghee	8	57	456	433	57	456	438
Meat	5	0	0	0	142	710	284
Vegetables	3	0	0	0	170	510	78
Salt	0	45	0	0	28	0	0
Turmeric	0	15	0	0	28	0	0
Total		...	3,907	3,922	...	14,131	4,200
Vitamin/Calories		1.00			3.36		
Body weight for which the VIT/CAL is adequate		36 kgm.			118 kgm.		

this ration depended almost entirely on the quality of the rice, and we have seen that this may vary considerably.

Following the introduction of a new ration in 1901 no more cases of beriberi were reported at Trincomalee. Inspection of Table 54 reveals that between three and four times as much vitamin B was provided in the new diet as compared with the old ration. The VIT/CAL ratio was raised to 3.26 or more, making the dietary adequate for all body weights including the maximum of the species, namely 115 kgm.

More recently—1911–1914—beriberi appeared at LeBong in British troops from England. It is unfortunate that Kennedy (1915), in his interesting account of this, did not record the diets in sufficient detail to allow calculations of vitamin content to be made. It is significant, however, that he did report many of the beriberic individuals as complaining that they could not eat the meat which was furnished. This, together with the fact that most of the men had suffered from diarrhea for a considerable period, or had been hospitalized shortly before for malaria, doubtless accounts in considerable measure for the appearance of beriberi at LeBong. For a more extended discussion of the relation of diarrhea and malaria to the development of beriberi see Chapter XIV, p. 208 *et seq.*

Philippine Scouts, 1908–1910

The "Philippine Scouts," constitute the native constabulary of the Philippine Islands. They consist of about 5,000 native soldiers organized into infantry units. The commissioned officers are Americans detailed for such service. The entire organization is under the control of and is supported by the War Department of the United States, and is distributed among many small garrisons throughout the Philippine Archipelago.

Prior to 1911 beriberi always appeared among these troops in sufficient numbers to constitute a serious problem. The incidence of this disease is shown in Table 55 taken from Vedder's (1913, p. 178) collection of statistics.

The prevalence of beriberi in the Philippine Scouts led to an investigation by a board consisting of Captains Phalen and Kilbourne, who, on September 30, 1909, brought in a report recommending several changes in the ration. The dietary then in use is shown in Table 56.

TABLE 55

Beriberi in the Philippine Scouts, 1902–1912

(Vedder, 1913, p. 178)

YEAR	MEAN STRENGTH SURGEON GENERAL'S OFFICE	ADMISSIONS FOR BERIBERI	
		Number	Rate per 1,000
1902	4,826	598	124
1903	4,789	614	128
1904	4,610	334	75
1905	4,732	170	36
1906	4,759	176	37
1907	4,679	115	25
1908	5,085	618	122
1909	5,369	558	104
1910	5,422	50	10
1911	5,389	2	0.4
1912	5,463	3	0.6

TABLE 56

Philippino Ration According to the U. S. Army Regulations 1908, Paragraph 1220

Subsistence upon this diet over an extended period was associated with some beriberi.

DIETARY COMPONENT	AMOUNT DAILY	VITAMIN INDEX	VITAMIN CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Beef, fresh	340	5	1,700	680
Allowable substitutes for fresh beef:				
Bacon	227	18	4,086	1,578
Canned meat	227	5	1,135	454
Canned fish	340	4.5	1,530	340
Fresh fish	340	4.5	1,530	340
Flour	227	3	681	795
Allowable substitute for flour:				
Hard bread	227	2.5?	568	733
Rice	567	1.6	907	1,985
Potato	227	3.8	863	220
Allowable substitute for potatoes:				
Onions	227	2.7	613	111
Coffee, roasted and ground	28	0	0	0
Sugar	57	0	0	228
Vinegar	0.08 gill	0	0	0
Salt	18	0	0	0
Pepper, black	0.5	0	0	0
Baking powder, when in field	91	0	0	0

In his discussion of this ration Vedder pointed out:

It by no means follows, however, that this was the food always eaten by any one company for several reasons. During active campaigning the ration was frequently

reduced to rice and canned salmon. Again, some Scout companies were stationed in remote districts, where it was impossible to obtain ice, and therefore fresh beef could only be obtained on rare occasions (once or twice a month), while during the remainder of the time the meat component was substituted by fish or bacon. And in addition to these circumstances the regulations provided that "savings" could be made on several articles of the ration, and the money value of these savings could be applied to purchase other articles of the ration, or supplies from the market, for the purpose of adding variety to the mess. And finally the money value of articles so saved could be added to the company fund and be spent for entirely different purposes.

When the 1908 ration (Table 56) is examined with respect to vitamin B content by our method, the data presented in Table 57 are obtained. The basal diet with no substitutions yields a VIT/CAL value of only 1.04, which is inadequate to protect against beriberi. The average of all of the 15 possible combinations of foods, taking into account the use of various substitutes, is slightly higher, being 1.13, the lowest and highest values being 0.96 and 1.36. Inasmuch as the soldiers are not limited strictly to the ration as described, but have the opportunity of varying the mess by purchases of foods from local markets through company "savings," the results of our calculations can be only roughly approximate. They indicate quite definitely, however, that beriberi should exist among individuals subsisting on such a ration, and this agrees with the facts shown in Table 55.

TABLE 57

Vitamin B Content of the Philippino Ration Specified in the U. S. Army Regulations for 1908, Paragraph 1220

COMBINATION OF FOODS	VITAMIN CONTENT	CALORIES, APPROXIMATELY	VITAMIN / CALORIES
	mgm.-eq.		
Basal ration only—no substitutions	4,151	3,908	1.04
15 other possible combinations, using all allowable substitutes, average	4,398	3,893	1.13
Maximum and minimum values			0.96–1.36
Estimated vitamin/calorie requirement for men weighing from 45 to 55 kilograms			1.27–1.56

In March, 1910, the War Department prescribed a new ration for the Philippine Scouts in an endeavor to prevent beriberi. Table

58 gives the details of the new dietary. It will be noticed that the changes instituted by the Washington authorities consisted in substitution of undermilled rice for the polished variety, and the addition of the mongo bean and the camote, a yam allied to the sweet potato.

The vitamin content of the 1910 ration is shown in Table 59. According to these estimations this diet is just adequate for the

TABLE 58

New Ration for Philippine Scouts Prescribed in General Orders No. 24, War Department, U. S. Government, 1910

DIETARY COMPONENT	AMOUNT	VITAMIN INDEX	VITAMIN CONTENT	CALORIES, APPROXIMATELY
	grams		*mgm.-eq.*	
Beef, fresh	340	5	1,700	680
Allowable substitutes for fresh beef:				
Bacon	227	18	4,086	1,578
Canned meat	227	5	1,135	454
Canned fish	340	4.5	1,530	340
Fresh fish	340	4.5	1,530	340
Flour	227	3	681	795
Substitute allowed:				
Hard bread	227	2.5?	568	733
Rice, Filipino no. 2*	454	3†	1,360	1,589
Substitute allowed when Filipino no. 2 cannot be obtained:				
Rice, Saigon	454	1.6	726	1,589
Mongos‡	113	26	2,938	394
Camotes§	227	3	681	279
Coffee, roasted and ground	14	0	0	0
Ginger root	14	2	28	7
Sugar	57	0	0	228
Salt	18	0	0	0
Pepper, black	0.5	0	0	0
Vinegar	0.08 gill	0	0	0

* An undermilled rice.
† Suggested by E. B. Vedder; personal communication.
‡ Mongo, or katjang idjo (Phaseolus radiatus Linn.), is a bean.
§ Camote is a yam vegetable allied to the sweet potato.

Philippine Scouts but with a very small factor of safety against beriberi.

Vedder (p. 177–180) describes the attempts which were made to apply the 1910 ration to the Scouts. Some difficulty was encountered in securing a satisfactory sample of undermilled rice.

> The camotes did not keep well, and neither they nor the mongos could always be obtained in sufficient quantities in the island markets. . . . Neither mongos nor

camotes met with favor as constant articles of diet. This order was, therefore, revoked by the War Department on November 7, 1910, and the ration reverted to its original status. There was, however, so much Filipino No. 2 rice on hand in the depots that its issue continued until June 1911. On this date the ration was finally prescribed, and was practically the same as the old Filipino ration, except that undermilled rice was ordered and Scout organizations were required to use the entire allowance of meat, and not more than 16 ounces of rice per day, and 1.6 ounces of beans per ration had to be consumed. It will thus be seen that after November, 1910,[1] there was a period of at least five months when the ration was exactly the same as the old ration which produced so much beriberi (Table 56), except that undermilled rice was issued, and that after June, 1911, it was the same ration except that both undermilled rice and beans were compulsory.

TABLE 59

Vitamin B Content of the New Philippine Scout Ration Prescribed in General Orders No. 24, U. S. War Department, 1910

COMBINATION OF FOODS	VITAMIN CONTENT	CALORIES, APPROXIMATELY	VITAMIN / CALORIES
	mgm.-eq.		
Basal ration only—no substitutions	7,388	3,972	1.99
15 other possible combinations, using all allowable substitutes: average	7,430	4,027	1.85
Minimum and maximum values			1.65–2.01
Estimated vitamin/calorie requirement for men weighing from 45 to 55 kilograms			1.27–1.56

Chamberlain (1911) attempted to correlate the incidence of beriberi with the use of the camotes, mongos and undermilled rice, and published interesting tables showing that the foods most effective against this disease seemed to be the undermilled rice and the mongos; the camotes and ginger roots apparently had but little protective action. It is not possible to calculate the vitamin contents of the dietary as affected by these changes described in Chamberlain's paper. An attempt has been made, however, to ascertain by our method the amount of vitamin present in the ration finally used after June 1911, when the incidence of beriberi became practically nil. Vedder states that this diet was essentially the same as had been used previously (Table 56) except that undermilled rice was used, 1.6 ounces of beans were consumed daily, and "savings" on the meat component were not permitted.

1. Vedder gives November, *1911*, which is obviously a misprint.

In Table 60 are shown the results obtained when our method for estimating vitamin B content is applied to such a diet. In making these estimations it should be borne in mind that a very low index was used for undermilled rice; in actual practice, the rice samples doubtless varied considerably in vitamin B content. According to these calculations the ration in use after June, 1911, was just barely adequate or was borderline with respect to furnishing an adequate amount of vitamin B, but markedly superior to the diet in use in 1908 and 1909, when beriberi was rife. If an index of 5 is used for undermilled rice, then the basal ration, without substitutions of any kind, has a VIT/CAL value as high as 1.83, which is more than adequate for these men.

TABLE 60

Vitamin B Content of Diet of Philippine Scouts in Use After June, 1911

COMBINATION OF FOODS	VITAMIN CONTENT	CALORIES, APPROXIMATELY	$\frac{\text{VITAMIN}}{\text{CALORIES}}$
	mgm.-eq.		
Basal ration—no substitutions	5,802	3,672	1.58
15 other possible combinations of the foods, using all allowable substitutes: average	5,909	3,686	1.61
Minimum and maximum values			1.31–1.79
Estimated vitamin/calorie requirement for men weighing from 45 to 55 kilograms			1.27–1.56

Application of the new method for calculating vitamin B contents of foods to these diets of the Philippine Scouts reveals, then, that the diet in use in 1908–1909 should have permitted considerable beriberi, which is in accord with the facts that an epidemic occurred in these years. The new ration ordered by the War Department in 1910, and used only a short time, was adequate in vitamin content and should have prevented the appearance of the disease. The dietary finally adopted in June, 1911, was just adequate, or borderline with respect to furnishing a sufficient amount of vitamin, but the calculation is less accurate in this instance, because of lack of knowledge as to the correct index to use for undermilled rice. The studies of Vedder and Feliciano (1928), and Aykroyd (1932) of the effect of milling on the vitamin B content of rice, agree in indicating that slight differences in the milling process

produce significant changes in the vitamin B content of the resulting product. It is very difficult, therefore, to make any really accurate estimation where an undermilled rice is employed.

British Troops During the World War

In the Mediterranean Area

In the recent monograph of the British Medical Research Council (1932) four diets are described in some detail as having been issued to a camp of British soldiers in the Mediterranean Areas during the World War. Two of the rations were associated with beriberi; the other two are described as having been adequate with respect

TABLE 61

Dietaries of British Troops in the Mediterranean Area as Described by the Medical Research Committee

(Special Report Series No. 38, London, 1919, Chapter IV, pp. 49–68)

CATEGORY OF INTEREST	ASSOCIATED WITH BERIBERI		NOT ASSOCIATED WITH BERIBERI	
	Diets		Diets	
	A 1	*A 2*	*B*	*C*
Total vitamin per week in *mgm.-eq.*	29,921	46,913	43,447	48,838
Total calories per week	30,750	30,782	25,102	25,361
Vitamin/Calorie ratio	0.97	1.52	1.73	1.93
Body weight for which this VIT/CAL value is just adequate (*kgm.*)	34	54	64	68
Average body weight of soldiers taken as (*kgm.*)	66	66	66	66

to their potency in preventing the development of this disease. It becomes of interest to determine how these diets compare in vitamin B content when examined by the method described in these pages. Calculations have therefore been made. Table 61 presents a summary of the categories of interest.

According to these results diets A 1 and A 2, both of which were associated with beriberi, were indeed deficient in vitamin B; ration A 2 was definitely superior to A 1, but, according to our estimate of the human requirement for the vitamin, was still definitely inadequate. Diets B and C should doubtless be classified as borderline, or as characterized by only a very slight factor of safety. No information is available to the writer as to how long these diets were

fed; with the vitamin content so close to the daily requirement in these cases, it is evident that a much longer period would be needed for use of these rations to result in beriberi. It seems more than a coincidence, that diet A 2 should have allowed beriberi whereas ration B did not, and that the value of the VIT/CAL ratio in the deficient ration should have been so close to that of the other, which represents practically the daily minimum for these soldiers.

At the Siege of Kut-El-Amara

According to Hehir's (1919) report, there were several outbreaks of beriberi among the British Troops in Mesopotamia in 1915–1916, particularly at the siege of Kut-El-Amara.

> The great majority of cases occurred within the first three months of the siege, that is, at the time when the mess, as regards quantity and variety, were seemingly better fed than during the later stages. The siege lasted from December, 1915, to 29th April, 1916—148 days. The disease gave rise to 155 admissions, all in British Troops. These were the continuation of a somewhat alarming outbreak of beriberi that began in Aziziyeh, after the first battle of Kut-El-Amara, early in October, 1915. The first lot of cases occurred after the retirement from Ctesiphon; a recrudescence took place at the end of January and in February, 1916. The onset of the disease was precipitated or, when already present, accentuated by marching or any kind of severe continuous exercise; in a number of cases it was preceded by diarrhea or some form of gastrointestinal disturbance.

Hehir also quoted, from the Medical and Sanitary Report of the Defense of Kut-El-Amara, what proves to be a very interesting paragraph in relation to the problem under consideration.

> In the early stage of the siege a recrudescence of beriberi amongst British Troops gave rise to some apprehension, but it then disappeared; whilst in Indian Troops and followers during the latter half of the siege, scurvy caused anxiety. The British Troops in the garrison received a cereal ration of wheaten flour during the first two months of the siege. From the 5th of February from one-third to one-half of the white wheaten flour was replaced at first by atta, and then by barley flour. The outbreak took place while on their normal ration of wheaten flour, and disappeared when they were compelled to use the coarser atta and barley.

Three diets are given in Hehir's paper. The ration issued January 22, 1916, may be taken as indicative of the dietary in use when the recrudescence of beriberi took place as described by Hehir. On February 5, 1916, this diet was changed, the coarser bread made with atta and barley being substituted for the white bread. The

rations issued March 4th and March 16th evidently represented adjustments to a failing food supply, but, according to the medical report cited above, were not associated with beriberi; the outbreak began to subside after February 5th when the change in bread was made. Each of these rations has been examined for vitamin B content by the new method. A summary of the findings of interest is presented in Table 62.

TABLE 62
Rations of British Troops at the Siege of Kut-El-Amara

TROOPS USING RATION	CATEGORY OF INTEREST	RATIONS ISSUED: January 22, 1916	February 5, 1916	March 4, 1916	March 11, 1916
British Troops	Total Vitamin per day in milligram-equivalents	3,944	4,931–5,611	5,924	5,660–6,228
	Total Calories per day	2,839	2,835	2,420	2,304
	Vitamin/Calorie ratio	1.39	1.74–1.98	2.45–2.60	2.46–2.70
	Body weight for which lowest value of VIT/CAL is just adequate (*kgm.*)	49	61	87	87
	Average body weight of soldiers taken as (*kgm.*)	66	66	66	66
British Indian Native Troops	Total Vitamin per day in milligram-equivalents	8,706	8,706	5,232–11,367	4,592–9,987
	Total Calories per day	2,843	2,843	2,149–2,603	2,208
	Vitamin/Calorie ratio	3.06	3.06	2.41–4.36	2.31–4.52
	Body weight for which lowest value of VIT/CAL is just adequate (*kgm.*)	108	108	85	83
	Average body weight of soldiers taken as (*kgm.*)	56	56	56	56

The January 22nd diet for the British troops was definitely deficient in vitamin B according to these estimations, and therefore should have been associated with beriberi, as is indeed the fact. The ration issued February 5th is very slightly deficient, if we base our comparison solely on the *minimum* value of the VIT/CAL ratio which the diet could have, namely, 1.74; it will be noticed that the value of this ratio could be anywhere between 1.74 and

1.98 and the average is practically identical with the estimated requirement of these men. From these considerations it appears that the diet was just adequate. Both of the diets issued in March prove to contain sufficient vitamin B, and therefore should not have been associated with beriberi; this agrees with the facts.

It is interesting to see that the rations used with the Indian Native Troops had large factors of safety and therefore should have prevented beriberi. This agrees with the fact that the disease did not occur among these troops.

U. S. Garrison, San Juan, Porto Rico, 1918

Ashford (1922) has discussed the incidence of polyneuritis among the United States draft troops recruited from Porto Rico in 1918. This polyneuritis was not officially designated beriberi until 1922. Investigation revealed several interesting facts concerning the ration of these draft soldiers.

> Polished rice was a staple article of diet during September, October and November, 1918. 2. It was served on an average of twice a day in that period. 3. There was a deficiency in fresh vegetables owing to local conditions. 4. The only vegetables served in large quantities were potatoes and the different varieties of beans. 5. A large amount of canned meats and vegetables were used, particularly by the company which yielded the majority of the cases.
>
> On questioning of the patients suffering from this polyneuritis it was discovered that those affected were rice eaters and consumed the full rice component daily. Most of the men did not eat the meat component and those who did ate sparingly of it.

In a table Ashford reported the average amounts of various foods consumed per man per day for September, October and November, 1918. An estimation, by our own method, of the vitamin B intake obtained from such a dietary, reveals that it should have been adequate, even allowing the substitution of rice for the meat component. The ration, as presented by Ashford, is found to have a VIT/CAL ratio of 2.87; with rice used to replace the meat, the value of this ratio becomes 2.34, which is considered to be just adequate for a man weighing 83 kgm. The average weight of these soldiers is estimated to be 62 kgm. (Davenport and Love, 1921).

Appointed to make an investigation, Ashford proceeded to obtain as accurate information as possible concerning food intake by

arranging for weighing of all food consumed by certain groups. Data were obtained from three companies covering the period June 1 to 10, 1921, inclusive. These have been submitted to our method of analysis for vitamin B content. A summary of the findings of interest is presented in Table 63.

According to Table 63, the VIT/CAL ratio of the diet actually consumed by Company A was such, that when rice was substituted for the meat, the diet was markedly deficient in vitamin B, and therefore might have allowed beriberi to develop. In the other companies, according to our calculations, a slightly greater factor of safety existed against this disease. Ashford does not indicate what

TABLE 63

Dietaries of U. S. Garrison at San Juan, Porto Rico

(Data of Ashford, 1922, pp. 312–313)

CATEGORY OF INTEREST	COMPANY		
	A	*D*	*Howitzer*
Vitamin/Calorie value:			
Of diet as described by Ashford, with no substitutions	2.10	2.30	2.25
With rice substituted for the meat	1.47	2.07	2.10
Body weight for which the lowest value of Vitamin/Calorie ratio is just adequate (*kgm.*)	52	73	74
Average body weight of these soldiers taken as* (*kgm.*)	62	62	62

* Davenport and Love, 1921, p. 125.

particular company furnished most of the cases of beriberi. One may regard these three company diets as indicative of the possibilities with respect to the choices of foods made by different mess sergeants and mess officers who are in direct charge of feeding the troop units. From Table 63 it is evident that poor selections of foods can be made by such officials even under normal conditions.

Ashford attempted to evaluate these diets with respect to vitamin B content by applying Eddy's (1921) table which indicates by plus signs the relative values of different foods as sources of vitamin B. Data were collected showing the daily food consumption of five companies over the period January 1 to April 30, and these were compared with data obtained from three companies over the first ten days in June. Concerning these two rations Ashford stated:

The ration, therefore, in June seems to be richer in anti-neuritic substances than that in the period January to April inclusive. As it was in the latter period or shortly thereafter that the most of the cases under consideration developed, it seems to be more than a coincidence that at that time the food was less rich in protecting substances.

Analysis of these two rations for vitamin B by our new method gives the results which are presented in Table 64, and which confirm Ashford's opinion expressed above.

TABLE 64

Dietaries of U. S. Garrison at San Juan, Porto Rico

(Data of Ashford, 1922, p. 315)

FOOD	VITAMIN INDEX	AVERAGE PER MAN PER DAY JANUARY–APRIL, 5 COMPANIES			AVERAGE PER MAN PER DAY IN JUNE, 3 COMPANIES		
		Amount	Vitamin content	Calories, approximately	Amount	Vitamin content	Calories, approximately
		grams	*mgm.-eq.*		*grams*	*mgm.-eq.*	
Rice	1.6	217	348	763	155	249	545
Beans	20	48	960	171	99	1,980	355
Potatoes	3.8	283	1,036	275	435	1,652	361
Onions	2.7	52	141	26	32	86	16
Meat, fresh	5	179	895	358	223	1,117	446
Fruits and vegetables	3	273	818	125	347	1,041	159
Totals		...	4,198	1,718	...	6,125	1,882
Vitamin/Calorie		2.44			3.25		
Vitamin/Calorie substituting rice for meat		2.01			2.77		
Body weight for which lowest value of VIT/CAL is just adequate (*kgm.*)		70			98		
Average body weight of these soldiers taken as (*kgm.*)		62*			62		

* Davenport and Love, 1921, page 125.

The factor of safety against beriberi, in the case of the January–April ration is extremely small, especially if it is remembered that the body weight of the soldiers, namely 62 kgm., which is used as a reference in estimating the adequacy of the diet, is an average figure. In the case of the June dietary there is a large factor of safety.

It is possible that our predicted minimum is too low for such troops as these draft soldiers at San Juan, because of the operation of special factors which may raise the minimum level of vitamin intake. In his medical report of the situation prevailing in 1918, Gutierrez reported among other things, that "in 90.5 percent (of the polyneuritis cases) ova of *Necator americanus* were found." Although it has not been clearly demonstrated as yet, it is not beyond the realm of possibility, that serious infestation with hookworm operates to raise the level of minimum vitamin B intake. It is well known that the presence of a tapeworm in the intestinal tract of man and animals interferes with proper nutrition. Test of this possibility with experimental animals should be made.

From these studies, it appears that the observations of beriberi among the troops at San Juan, Porto Rico, are not inconsistent with the thesis here advanced. Application to the San Juan rations of the new method for estimating the vitamin B content of human dietaries reveals that the development of beriberi was quite possible under the conditions described. The analyses of these diets also indicate why the disease was not more prevalent than it really was. In all but one of the rations studied, the factor of safety was great enough to constitute a reasonable insurance against beriberi.

Congo State Railway Construction, 1892

Braddon (p. 272 *et seq.*) gives a translation of part of the official account by Bourguignon, Dryepondt, and Firket (1897, 1898) of the causes of mortality on the Congo during the construction of the railways there:

During the first years of construction the ration (of the native coolies) was composed of:

Rice	750 grammes.
Mossamedes dried fish	250 "

These articles were as a rule of satisfactory quality; the rice was at times broken, but the Medical Department were careful to reject altered and sticky lots, which sometimes were offered. The chief fault of this ration was its monotony, the coloured labourers finding it very difficult at that time to get fresh provisions by barter in the district where the first works were carried on.

Now, the fearful mortality which prevailed among the coloured men employed on the works in these first years is notorious. Negroes from Barbadoes, Chinese, Guinea-Coast-men fell victims by tens of thousands (*milliers*) to malarial cachexia

and beriberi. In two months of 1892 the death rate among them rose to 75 percent per mille per month, which would have given the unheard of total of 900 per 1,000 per annum had the conditions persisted. At that juncture the mortality among the coloured was seven or eight times greater than among white men. The latter resisted better because they were better lodged and better fed; what was wanted, therefore was to increase the resistance of the blacks. So, to oppose the calamity, drastic alterations were quickly brought about in the conditions of the workmen's living.

The actual regimen adopted by the railway company for its negro labourers now comprises for the daily ration one fixed component—rice, and four articles varying day by day. Each negro coolie gets daily:

Rice	500 grammes	(constant)
Dried fish	250 "	variable
Salt meat	250 "	variable
Beans	250 "	variable
Delacre biscuits	250 "	variable

These elements are combined so as to have rice, salt meat, and biscuits, or rice, fish, and beans, together, etc., the total allowance amounting to 1,000 grammes per head. At certain times 60 to 100 grammes of lard or palmoil are added, with salt and native pimento (pili-pili).

At the same time, the progress of the work, which had at length passed the gorge of Mpozo and the Palaballa ridge, afforded opener ground for camping, and—a matter of importance from the sanitary point of view—the smoother progress gave opportunity to shift camp earlier, so as not to dwell long upon sites where soil became speedily polluted.

The housing of the labourers was improved by getting large waterproof tents, supplied by one of the best makers. Finally, a system of bounties to the men, according to the task performed, stimulated their industry, the negroes working harder, and with the profit used their extra pay to buy preserved milk, bread, or tinned European meats. Under the influence of these different conditions, the mortality quickly fell; notwithstanding the dangers inherent in great works of clearing and excavation in the tropics, it came down to about 50 per 1,000. What a contrast with figures given above, etc.

In Table 65 are presented estimates of the vitamin B content of the diets fed to these negro labourers. Diet I is the ration which was being fed when the mortality during two months of 1892 reached 750 per 1,000 *per month*. Diet II, as presented in the table, consists of the six possible combinations of rice, dried fish, meat, beans, and biscuits. Examination of the last column of the table, in which are listed the values of the VIT/CAL ratio, indicates that some of these combinations were much better than others. In view of present-day knowledge, this might be expected. The average of these combinations has also been calculated; this gives the datum which may properly be compared with that for Diet I.

The value of the ratio VIT/CAL for Diet I is only 0.97. Reference to Chart 6 (p. 110) shows that this is just sufficient for a body weight of 37 kgms. or 81 pounds. The average weight of the

TABLE 65

The Vitamin B Content of the Diets Fed to Negro Laborers Engaged in Railway Construction in the Congo State, 1892

(Braddon, 1907, p. 272 *et seq.*)

DIET		COMPONENT	AMOUNT	VITAMIN INDEX	VITAMIN B CONTENT		CALORIES, APPROXIMATELY	$\frac{\text{VIT}}{\text{CAL}}$
					Food	Total		
			grams		*mgm.-eq.*	*mgm.-eq.*		
I		Rice	750	1.6	1,200			
		Dried Fish	250	8	2,000	3,200	3,295	0.97
II		Rice	500	1.6	800			
	(a)	Dried Fish	250	8	2,000			
		Meat	250	5	1,250	4,050	2,778	1.46
		Rice	500	1.6	800			
	(b)	Dried Fish	250	8	2,000			
		Beans	250	23	5,750	8,550	3,178	2.69
		Rice	500	1.6	800			
	(c)	Dried Fish	250	8	2,000			
		Biscuits	250	2	500	3,300	2,918	1.13
		Rice	500	1.6	800			
	(d)	Meat	250	5	1,250			
		Beans	250	23	5,750	7,800	3,105	2.51
		Rice	500	1.6	800			
	(e)	Meat	250	5	1,250			
		Biscuits	250	2	500	2,550	2,855	0.89
		Rice	500	1.6	800			
	(f)	Beans	250	23	5,750			
		Biscuits	250	2	500	7,050	3,255	2.17
Totals						36,500	21,384	av. 1.69
$\frac{\text{Vitamin}}{\text{Calories}}$						1.71		

Diet I: VIT/CAL of 0.97 just adequate for body weight of 37 kgm.
Diet II: VIT/CAL of 1.70 just adequate for body weight of 60 kgm.
Probable average body weight of negro laborers: about 62 kgm.

negro labourers was probably not far from 136 pounds, or 62 kgm. (This, incidentally was the figure given by Davenport and Love (1921) for U. S. Army recruits in 1917 of Cuban, Spanish, and West

Indian origin.) It is obvious that subsistence on Diet I for a sufficiently long period should have resulted in an epidemic of beriberi, which indeed occurred in the Congo State. It will be remembered, also, that the official account mentioned the incidence of malaria, which would doubtless have raised the requirement for vitamin B (see Chapters VIII and XIV).

The average value of the VIT/CAL ratio in the case of Diet II is 1.70. This proves to be just adequate for a man weighing 60 kgm. (see Chart 6, p. 110). The ration was probably slightly better than this figure indicates, at least for some of the negroes, because, as stated in the official account, institution of a "system of bounties to the men, stimulated their industry, according to the task performed, the negroes working harder, and with the profit used their extra pay to buy preserved milk, bread, or tinned European meats." It appears, then, that the new diet provided just the minimum amount of vitamin for individuals of about average body weight, with no factor of safety; the heavier men had no factor of safety whatever. Under these conditions, therefore, one could hardly expect the beriberi to have completely disappeared, as indeed it failed to do.

Lascars and Other Native Seamen on British Ships

Braddon (1907, p. 451) records that "the majority of recorded epidemics of beriberi on British ships occur among Lascar crews," and gives the details of the dietary provided these sailors by the British Board of Trade Regulations. A calculation of the vitamin B content of this dietary is presented in Table 66.

From the data presented in this table it is evident that the diet is borderline with respect to supplying sufficient amounts of vitamin B; certainly the factor of safety against beriberi is very small. The diet is adequate, according to the formula, for men weighing 58 or 59 kgm., which is very close to the highest body weight characteristic of these sailors. From this it is obvious that any failure to provide over an extended period the proper supplements to the rice, which forms the staple food, courts the development of beriberi. It is very reasonable to expect that beriberi should develop from time to time among sailors subsisting on this ration, which appears to have been the case.

TABLE 66

Vitamin B Content of the Diet Provided Lascars and Other Native Seamen on British Ships according to the British Board of Trade Regulations

"The majority of recorded epidemics of beriberi on British ships occur among Lascar crews." (Braddon, 1907, p. 451.)

FOOD	AMOUNT PER MAN PER DAY	VITAMIN INDEX	VITAMIN CONTENT	CALORIC INDEX	CALORIE CONTENT
	grams		*mgm.-eq.*		
Rice	680	1.6	1,088	3.51	2,387
Dhal	113	26	2,938	3.49	394
Ghee	57	8 (?)	456	7.69	438
Fresh meat (in harbor)	284	5	1,420	2.00	568
Vegetables	227	4*	908	0.70	159
Salt fish (at sea)	113	8	904	3.00	339
Lime juice (after 10 days from port)	28	3	84	0.48	12
Salt, tea, etc.	...	....	.....	0	0
Sugar	30	0	0	4	120

	VITAMIN	CALORIES	VIT/CAL
Totals in harbor	6,810	4,066	1.68
at sea	6,378	3,849	1.66

Body weight for which these values of the ratio are just adequate	58–59 kgm.
Probable body weights of sailors	40–60 kgm.

* Considered as including tubers (potatoes, taro, etc.) and therefore having a value of 4 rather than 3.

Summary of the Study of Diets Associated with Beriberi

As one type of test of the new formula by which man's requirement for vitamin B is estimated, the rations, used by 19 groups of individuals among whom beriberi appeared, have been evaluated with respect to their content of this vitamin. In this work 180 different combinations of foods were studied (see Table 67). The data presented in the last column of this table are of greatest interest because they indicate to what extent the vitamin B contents of these various diets satisfied the human requirement for this dietary factor as shown by the presence or absence of beriberi. It will be noticed that the four diets associated with beriberi, as described by Megaw and Bhattacharjee for groups in Calcutta, India, fail to support the thesis being advanced. As was pointed out previously, many of the individuals in these Calcutta groups were reported as suffering from malaria or marked diarrhea, and therefore might be

TABLE 67

The Vitamin B Contents of Diets Associated with Beriberi, or Used to Bring About a Disappearance of the Disease

Summary Table

CLASSIFICATION OF GROUP	LOCATION OF GROUP	NUMBER OF DIETS EVALUATED	DO THE RESULTS OF THE DIETARY ANALYSIS AGREE WITH THE FACTS CONCERNING THE INCIDENCE OF BERIBERI?
Families	Newfoundland and Labrador (Aykroyd)	25	Yes
	Calcutta (Megaw and Bhattacharjee)	7	Poor: 4 beriberi diets higher in vitamin content than predicted minimum.
Beriberi Experiments on Human Beings	Wright's "correct diet" (Pudoh Gaol)	1	Yes
	Fletcher: Kuola Lumpur	2	Yes
	Frazer and Stanton	2	Yes
	Strong and Crowell: Bilibid Prison Volunteers	17	Yes
Public Institutions	Selangor Gaols, 1892–1902	19	Yes: two exceptions where beriberi diet higher in vitamin content than predicted minimum.
	Singapore Prison, 1869–1901	10	Yes: two exceptions where beriberi diet higher in vitamin content than predicted minimum.
	Bilibid Prison, Manila, Epidemic, 1901–1902	3	Yes
	Java Prisons: Vordermann Data	1	Yes
	Richmond Asylum, Dublin, 1897	1	Poor: calculation shows diet borderline, but beriberi occurred in epidemic proportions.
Military and Naval Organizations	Dutch East Indian Navy, 1870–1880	6	Yes
	Japanese Navy (Takaki), 1883–1884	5	Yes
	Boer Prisoners, St. Helena, 1901–1902	1	Yes
	Indian Native Troops, Madras, 1898–1901	5	Yes
	Philippine Scouts, 1908–1911	48	Yes
	British and Indian Troops, World War	12	Yes: with one questionable exception, adequate diet calculating as borderline in vitamin B content.
	U. S. Troops, San Juan, Porto Rico, 1918	8	Yes
Miscellaneous	Congo Railway, 1892	7	Yes
Total		180	

regarded, for these reasons, as having a higher vitamin B requirement. Furthermore, the amounts of the components of the rations were expressed in only roughly approximate quantities and therefore calculations based upon them would be expected to yield results less accurate than might be desired. It is recognized that a critic may regard these considerations as of little import or, on the other hand he may even cite these Calcutta data as failing definitely to support the thesis here advanced.

The other instances of only fair agreement may be summarized briefly. Two of the rations used in the Selangor Gaol show poor agreement; in the case of the one showing the greatest failure the discrepancy is about the same as the smallest one observed with the Calcutta group; and with both of these Selangor diets the associated incidence of beriberi was very slight. With respect to the two Singapore prison diets cited as showing only fair agreement, it may be pointed out that the factor of safety against beriberi in the case of one of these was extremely small; in fact both of these diets might fairly be considered as borderline with respect to supplying sufficient vitamin B. The ration of the Richmond Asylum, Dublin, also calculates as having been borderline, but the disease occurred in epidemic proportions; therefore the agreement in this case is recorded as poor. One of the diets used by the British Troops in the Mediterranean Area during the Great War calculates as just barely adequate, or borderline, although the ration is reported in the literature as not having been associated with beriberi. No information is available as to how long the soldiers subsisted on this dietary, whether the period was long enough to demonstrate unquestionably that the diet was adequate.

When one attempts to express in numerical fashion the extent of agreement of these findings with the thesis being advanced, an interesting result is obtained (See Table 68). 180 separate combinations of foods were evaluated in this phase of the investigation. With certain groups, the Philippine Scouts, for example, many substitutes for certain components of the ration were allowed, and therefore many calculations were necessary in order to obtain a reasonably clear idea as to the probable vitamin B intake. If the averages considered as fairly representative of the different groups be taken, rather than the entire 180 separate food combinations

studied, a total of 116 diets results. Of this total 10 of the calculations (last columns of Table 68) may be considered as failing to agree well with the facts concerning the incidence of beriberi, or 8.6 percent. Considering the nature of the phenomena studied, the assumptions which are necessary when making calculations of diets used many years ago, and the extent to which numerous biological functions are known to vary in perfectly normal subjects, a failure of these calculations to agree with our favored view in only 8.6 percent of the cases is believed to constitute excellent support of the thesis being advanced. To many readers, doubtless, an 8 percent failure of agreement of fact with theory may seem too large. It is pertinent to remind them, however, that the basal metabolic rate of

TABLE 68

Diets Evaluated For Vitamin B Content in Relation to Presence of Beriberi

(a) Food combinations which were associated with beriberi	137
(b) Food combinations associated with disappearance of beriberi, or which were used by groups comparable to those in (a)	43
(c) Total food combinations evaluated in this phase of the study	180
(d) Total food combinations corrected for duplications, substitutes allowed in different rations, etc.	116
(e) Cases not agreeing well with predicted human need for vitamin B—see last column Table 67—number	10
Percent of (d)	8.6

normal individuals, for example,—a biological function regarded as being quite constant and which can be measured with an accuracy of less than two percent—has been shown to vary in the same person in a given 24 hour period by as much as 8–10 percent, and in a group of 104 normal individuals of the same sex (Harris and Benedict, 1919) by as much as 9.1 percent. In view of such considerations as these, therefore, the writer believes that the agreement of these findings, concerning the vitamin B contents of the diets and the incidence of beriberi, with the predictions as to the human requirement for this vitamin is very good. This agreement supports the conclusions: (*a*) that the new formula states man's quantitative need for vitamin B with reasonable accuracy, and (*b*) that it is now possible to evaluate human dietaries with respect to their content of this important dietary essential.

CHAPTER XIII

THE VITAMIN B CONTENT OF DIETS NOT ASSOCIATED WITH BERIBERI

THE 180 food combinations evaluated and described in the preceding chapters were used by persons either afflicted with or recovering from beriberi, or by healthy individuals considered as properly to be compared with these beriberi patients. If the author's thesis is correct, it is clear that examination of diets known to be associated with *absence* of beriberi should show that these rations contain amounts of vitamin B more than adequate to meet the human requirements. As a test of this proposition 216 "good" diets have been evaluated for vitamin B content. The results of this phase of the investigation will now be presented.

American Diets

American White Families

Sherman (1924) has given a table representing the "average American diet" and showing the types of food, cost, and the composition in terms of calories, protein, calcium, phosphorus and iron. This average diet is the result of a study of 92 American family dietaries, each recorded over a period of at least one week. Sherman groups certain foods under appropriate headings such as "meats and fish," "grain products," etc. Calculations for vitamin content of such items would necessarily be much less accurate if a vitamin index value for the group were used, because of the difficulty in arriving at the appropriate vitamin B index value to use. In such instances, therefore, the group total of calories has been distributed among different foods according to the proportions of these nutrients in the average American dietary as calculated by Langworthy (1907) from data available to the United States Department of Agriculture. For example, the total of "Meat and Fish" Calories as reported by Sherman is 16.54 percent of the daily total intake per capita. Langworthy furnishes data concerning the proportionate

consumption of beef, pork, lamb and mutton, poultry and fish. On the basis of Langworthy's data, the 16.54 percent of the daily calories has been distributed over these various kinds of meats as shown in column 2 of Table 69. For the purpose of this calculation the average man is assumed to weigh 66 kgm., for reasons indicated in Chapter XI (see page 111), and the daily caloric intake is taken as 2,500 Calories. In order to estimate the average daily intake of the different foods in grams, (Table 69, column 4) Sherman's factors of "grams per 100 Calories" (column 3 of Table 69) for the respective nutrients are used.

From the data presented in Table 69 it appears that this average American dietary affords a very liberal factor of safety against beriberi. The value of the VIT/CAL ratio proves to be 2.74, which is 50 percent greater than the estimated minimum value of about 1.82. This finding is in agreement with the observation that beriberi is exceedingly rare in the United States. Before deciding definitely, however, that the average American diet furnishes liberal amount of vitamin B, let us examine this matter more closely. An average value presupposes a variation, some values being above and some below the average. How great is the variation from the average value for the American diet? In order to answer this question separate calculations have been made with each of 121 diets of American Caucasian families described in detail in various U. S. government bulletins reporting the work of Atwater and his associates carried on between 1895 and 1899. The results of these estimations are summarized in Table 70. It appears that the mean value of the VIT/CAL ratio for these 121 families is 2.77, which is practically identical with the value yielded by the calculation based on the Sherman data. In 6 of the 121 families (5.4 percent) the value was below the estimated minimum of 1.82; in 8 instances the value was between 1.82 and 2.00, indicating a presumably low margin of safety against beriberi. These 14 cases, where the vitamin B intake might be regarded as unsatisfactory, constitute 11.6 percent of the total number studied.

In eight instances the original data concerning these 14 "doubtful" families include information as to the weights of the various members of the family. In such cases, therefore, it is possible to determine the true average weight to use in comparing the vitamin

TABLE 69

*Vitamin B Content of the Average American Diet as Described by Sherman (1924)**

FOOD AND PERCENT OF CALORIES CONTRIBUTED BY IT	CALORIES PER DAY	GRAMS PER 100 CALORIES	FOOD PER DAY	VITAMIN INDEX	VITAMIN CONTENT
(1)	(2)	(3)	(4)	(5)	(6)
			grams		
Meat and Fish: 16.54 percent *taken as***					
Beef	159	70	111	5	555
Pork, including lard	159	25	40	24	960
Lamb and mutton	21	45	9	5	45
Poultry	14	100	14	5	70
Fish	40	48	19	4.5	86
Eggs: 1.75 percent	42	76	32	5.5	176
Milk: 8.11 percent	193	145	280	3.6	1,008
Cheese: 0.94 percent	23	22	5	2	10
Butter and Fats: 10.29 percent	245	13	32	8	256
Grain Products: 37.79 percent *taken as*					
Wheat: patent flour	360	29	104	3	312
bread, crackers, etc.	189	38	72	2	144
sweet cakes	17	29	5	2	10
entire flour and graham	54	41	22	20	440
graham bread	26	38	10	10	100
Corn: meal and flour	256	28	72	5	360
preparations	55	28	15	2.5	38
Oatmeal and preparations	14	25	3.5	16	56
Rice	7	28	2	1.6	3
Rye, barley and buckwheat	42	28	12	3	36
Vegetables and Legumes: 9.03 percent *taken as*					
Legumes, dried	10	29	3	26	78
Legumes, fresh	7	100	7	10	70
Tubers and yams	133	100	133	3.8	505
Others	65	300	195	3.6	702
Nuts: 0.27 percent	7	15	1	18	18
Fruits: 3.87 percent	90	154	139	3	417
Sugar and Molasses: 10.78 percent	256	28	72	1	72
Miscellaneous: 0.65 percent	16	?	?	0	0
Total	2,500	...	.....	....	6,847
Vitamin / Calories					2.74

* Sherman, H. C., in *Chemistry of Food and Nutrition*, revised edition, 1924, p. 391.

** Where it has been necessary to distribute the group total of calories among different foods, the distribution has been made according to the proportions of these foods in the average American dietary as calculated by Langworthy in *Food and Diet in the United States*, Yearbook of the U. S. Department of Agriculture, 1907, pp. 361–378, particularly the table, page 375.

intake with the requirement rather than the average of large numbers of families as must be done otherwise. When these actual average weights are used and the estimate of the adequacy of these diets is based thereon, it appears that the diets of these families afforded even greater factors of safety than the data in Table 70 would suggest. These additional data are summarized in Table 71.

It will be noticed that, with the exception of Dietary Study #168, the differences between the VIT/CAL values of the diet as eaten and those expressing the predicted requirement—data in

TABLE 70

The Vitamin B Contents of Diets of American White Families Studied over Periods of at Least One Week

Summary Table

GROUP OF WHITE FAMILIES	NUMBER OF FAMILIES IN GROUP	VITAMIN/CALORIE RATIO			
		Average	Below* 1.82	From 1.82 to 2.00	Above 2.00
New York: 1896–1897	54	2.35	6	5	43
Chicago: 1895–1896	53	3.03	0	3	50
Tennessee, California, etc., families, 1896–1898	14	2.88	0	0	14
Total	121		6	8	107

Grand mean	2.77
Average deviation	0.51
Average deviation in percent of mean	18.4

* Assuming that a value of 1.82 represents the minimum compatible with protection against beriberi. Values between 1.82 and 2.00 may well be regarded as too close to the minimum to be satisfactory.

columns 5 and 6 respectively—were appreciable and therefore represented moderate factors of safety against beriberi; in the case of Study #168, the two values are so close as to indicate only very slight protection against the disease. The family represented by Study #168 consisted of a mother, 55 years of age, three daughters 22, 20 and 14 years old, respectively, and a 17 year old son.

When considering data of this nature it is pertinent to point out that the diets used by these families represent their food selections over periods of about a week; it is perfectly possible that other and better choices would be made during other weeks. The fact that the average ration of the American white family is as high as 2.77 indi-

cates that ample supplies of various valuable foods are readily available. Probably the chief factor operating to bring about poor choices of foods is the economic one. It seems rather surprising that, even with only small sums available for the purchase of foods, more of the families included in the group here studied should not have come closer to the minimum of vitamin B intake. This is probably due to the fact that it is very easy to improve a faulty diet under

TABLE 71

Further Details Regarding the White American Families Summarized in Table 70

	SOURCE OF DATA: U. S. DEPT. AGRIC.		AVERAGE WEIGHT OF FAMILY	VIT/CAL RATIO	VIT/CAL VALUE JUST ADEQUATE FOR THIS WEIGHT	FAMILY RESIDENT IN
	Bull. number	Dietary study number				
			kgm.			
Vit/Cal Ratio below 1.82	46*	34	Weight data not given "were small"	1.69	....	New York
	46	51	Not given	1.76	....	New York
	116†	168	55	1.68	1.56	New York
	116	194	43	1.78	1.20	New York
	116	196	42	1.61	1.18	New York
	116	201	37	1.71	1.06	New York
Vit/Cal Ratio between 1.82 and 2.00 inclusive	55‡	55	Not given	1.84	....	Chicago
	55	64	Not given	1.94	....	Chicago
	55	116	Not given	1.97	....	Chicago
	46	31	Not given	1.86	....	New York
	116	161	43	1.96	1.20	New York
	116	177	38	1.88	1.08	New York
	116	188	38	1.96	1.08	New York
	116	197	32	1.82	0.94	New York

* Atwater, W. O., and Woods, C. D., 1898.
† Atwater, W. O., and Bryant, A. P., 1902.
‡ Atwater, W. O., and Bryant, A. P., 1898.

the food conditions prevailing in the sections of the United States represented by these families. This is in marked contrast to the situation in the Philippine Islands and other localities in the Far East where extreme poverty is very widespread.

These studies of the diet used by the average American white family are obviously in complete agreement with the thesis here advanced. The fact that beriberi is quite rare in such families finds a simple explanation in these calculations of the amount of vitamin B furnished.

American Negro Families

Atwater and Woods (1897) and Frissell and Bevier (1899) collected data on the diets eaten by poor negro families in Alabama and eastern Virginia respectively. Although these groups subsisted under conditions of extreme poverty, they were free from beriberi. Search of the medical literature reveals that even to the present day beriberi is practically unknown among the poor negroes of Alabama and Virginia. The data regarding the foods eaten by these negro families thus acquire considerable interest, and therefore have been examined with respect to vitamin B content by the method described in this monograph.

TABLE 72

The Vitamin B Content of the Diets of Poor Negro Families in Eastern Virginia and Alabama, 1897–1898 and 1895–1896, Respectively, Studied Over Periods of at Least One Week

A Summary Table

GROUP OF NEGRO FAMILIES	NUMBER OF FAMILIES IN GROUP	VITAMIN/CALORIE RATIO		
		Mean	Average deviation	Average deviation in percent of mean
Alabama, 1895–1896*	20	3.63	0.56	15.4
Eastern Virginia, 1897–1898†	19	3.13	0.44	14.0
For entire group of 39 families		3.39	0.58	17.1

* Atwater, W. O., and Woods, C. D., 1897.
† Frissell, H. B., and Bevier, I., 1899.

A summary of the findings is presented in Table 72. From these data it appears that the diets provided a very large factor of safety against beriberi. The average value of the VIT/CAL ratio is 3.39 with a standard deviation from this of 22 percent (0.75). Thus, the value of the ration, in view of the standard deviation, might be as low as 2.54, or as high as 4.14. This large factor of safety against beriberi is readily explained by the relatively great consumption of low grade corn meal—essentially the whole grain—cheap pork sides, a common meat richer in vitamin B than any other that is available, and molasses, which rates quite high with respect to vitamin B content. It is an interesting and curious fact that the extremely poor families as a rule received more vitamin B in their diet

than families with slightly improved economic status. Evidently, the receipt of somewhat larger income was associated with an "improvement" (?) of taste in the matter of food selection, and various nutrients with actually a lower vitamin B content were chosen to supplement the very cheapest foods available. The staple foods, available to the poorest families, happen to be foods rich in vitamin B. This is in marked contrast to the situation in the Far East where the cheapest staple is a highly milled product, namely white, or polished rice. The results of these studies of negro diets thus harmonize readily with the author's point of view.

Various Special Groups in the United States, 1895–1898

In a group of research bulletins Atwater and his associates reported diets eaten by various groups throughout the United States during the period 1895–1898. These included a college football team, numerous college eating clubs, lumbermen working in the Maine forests, three persons who subsisted entirely on fruits, and who therefore might be called "fruitarians," an individual who was a vegetarian, four Mexican families, the family of a Chinese dentist in California, and two eating clubs of Chinese laundry and truck farm employees. These data have been analysed for vitamin B content by our method.

The dietaries of the football team and the college eating clubs probably reflect in large measure the food habits of American white families. The data obtained from the Maine lumbermen should be of special interest because of the fact that the daily caloric intake of the Maine lumberjack is very nearly, if not actually, the highest on record in the literature on human nutrition. The results with the vegetarian and fruitarians are interesting because of the food fads which are thus represented. The calculations in the cases of the Mexican families in the state of New Mexico and the Chinese groups in California give some indication of the extent to which the different and characteristic dietaries of these "foreign" groups in the United States afford a protection against beriberi. The findings for these various groups are summarized in Table 73.

With respect to the football team and the college eating clubs it will be noticed that the mean value of the VIT/CAL ratio is almost identical with that for the 121 separate American white fam-

ilies discussed in a previous section. The three separate studies carried out at the University of Tennessee (# 39, 40, 41) were made at the same club. The results, therefore, are specially significant be-

TABLE 73

The Vitamin B Contents of Various Diets Used in the United States During the Period 1895–1898

BULL. NO.*	DIETARY STUDY NO.	DESCRIPTION OF GROUP	VITAMIN/CALORIE RATIO: For the group	VITAMIN/CALORIE RATIO: Mean	VITAMIN/CALORIE RATIO: Average deviation in percent mean
184	268	College football team	2.40		
31	94	Eating Clubs: Univ. Missouri	2.23		
31	95	Eating Clubs: " "	1.90		
37	148	Eating Clubs: " Maine	2.42		
37	149	Eating Clubs: " "	3.61		
37	150	Eating Clubs: " "	4.64	2.78	20.9
37	151	Eating Clubs: " "	2.70		
37	152	Eating Clubs: " "	3.15		
29	39	Eating Clubs: " Tennessee	2.88		
29	40	Eating Clubs: " "	1.98		
29	41	Eating Clubs: " "	2.65		
149	390	Maine lumberman	3.12		
149	391	" "	2.36		
149	392	" "	2.20	2.28	16.3
149	393	" "	1.78		
149	394	" "	1.92		
132	355	Fruitarian, California	4.98		
132	362	" "	3.01	3.62	18.7
132	363	" "	3.37		
132	356	Vegetarian, "	3.13		
40	163	Mexican family, New Mexico, poor	3.15		
40	164	" " , moderate circumstances	1.78	2.79	17.9
40	165	" " , very poor	2.84		
54	225	" " , poor	3.37		
107	325	Chinese dentist's family, Calif.	3.68†		
107	326	" Laundry Assoc., Calif.	3.15†	3.25	32.5
107	?	" truck farm employes, Calif.	2.92†		

* Number of Bulletin of the U. S. Dept. Agriculture, Office of Experiment Stations, from which data for this calculation were obtained.
† This is a "not less than" value.

cause they indicate the extent to which the value of the VIT/CAL ratio may vary. Study # 40 was begun upon completion of # 39, and yielded the low value of the VIT/CAL ratio of 1.98, in con-

trast to 2.88, which was obtained in study #39. Study #41 was performed much later during a warm season, and yielded a result not appreciably different from the mean.

The dietaries of the Maine lumbermen show only one instance (study #393) where the value of the VIT/CAL ratio was as low as 1.78, which, according to our prediction chart (Chart 6, page 110) is dangerously close to the minimum. The fact, however, that the other values obtained with these lumberjacks were much higher, suggests that over an extended period the vitamin B intake would be great enough to prevent beriberi.

The vegetarian and fruitarian diets yielded a very liberal intake of vitamin B. The mean of the four dietaries here studied is 3.62, a value much higher than that characteristic of the diet of the average American white family. This is to be expected because fruits and vegetables, although relatively low in vitamin B content, must be eaten in unusually large amounts in order to furnish sufficient calories, something which the members of these groups of food faddists are willing to do; the VIT/CAL values of these foods are higher than those of most other classes of foods.

The dietary of the poor Mexican family includes appreciable quantities of beans and maize, and therefore furnishes quite liberal amounts of vitamin B. The mean value of the VIT/CAL ratio for these four Mexican family diets is almost identical with that of the average American white family previously described. It is interesting to see in this Mexican group the same phenomenon which characterized the negro families, namely the smaller amount of vitamin B furnished by the diet of the family with more improved economic status, namely study #164; in this case the value of 1.78 is quite close to the probable absolute minimum, and therefore represents, in our opinion, only a very slight protection against beriberi. The values characteristic of the other families of this group are much higher and suggest that appreciable variation in the selection of foods from that which obtained in study #164 would probably increase the vitamin B intake. So far as the medical literature indicates, beriberi has not been observed in Mexican families.

All of the values of the VIT/CAL ratio yielded by the Chinese dietaries studied here represent minima; the true values are undoubtedly greater. The reason for this lies in the fact that, for many

of the foods which these Chinese dietaries contained, vitamin B index values are not available. With this in mind it is especially interesting to find that even the lowest value here recorded, namely 2.92, is higher than the mean of the average American white family diet. This finding harmonizes with the fact that beriberi occurs only very rarely among Chinese who have been residents in the United States. The few cases of this disease that have appeared (see pp. 11) have occurred chiefly among oriental sailors arriving at American ports; these individuals have been restricted for a considerable period to a ship's ration, which may have afforded only very slight or no protection against beriberi.

From this brief review of miscellaneous American dietaries it is clear that the relatively large amounts of vitamin B which they furnished account for the almost complete absence of beriberi from the United States, which is a fact of record.

American White Family Receiving Food Relief in 1932 in Accordance with the Recommendations of a Trained Nutritionist

The diets which have just been reviewed were in use many years ago. It becomes of interest to determine whether rations in use more recently in the United States contain sufficient vitamin B. This is particularly true of families which have had to seek aid from relief agencies. The widespread economic depression, which began late in 1929, has resulted in an unusual number of such families, and consequently, considerable effort has been expended by students of nutrition to make sure that these families receive diets which are not only economical but adequate as well. In this connection Dr. Adelaide Spohn, working on this problem under the auspices of the Elizabeth McCormick Memorial Fund, Chicago, has furnished the author with detailed data showing the foods consumed by a family consisting of father, mother, boy 15 years old, girl 13, boy 4 and a girl 2 years old, respectively. The data covered the week of April 5 to 12, 1932. The food allowance was limited to \$8.45; the actual expenditure amounted to \$7.95. The cooking facilities of this family were limited to a two-burner gas stove without an oven. This fact had to be considered in planning the family menus. Dr. Spohn made her recommendations as to food purchases with the object of securing for the family adequate intake of energy,

TABLE 74

*Vitamin B Content of Diet of an American White Family Receiving Food Relief in Accordance with the Recommendations of a Trained Nutritionist**

FOOD	AMOUNT	VITAMIN INDEX	VITAMIN CONTENT
	grams		*mgm.-eq.*
Milk, fresh	13,650	3.6	49,140
Milk evaporated	3,840	3	11,520
Bread	8,400	2	16,800
Butter	226	8	1,788
Oleomargine	906	0?	0
Lard	453	11	4,984
Oranges	2,328	2.7	6,286
Prunes (corrected)	790	14	11,060
Bananas	600	2.9	1,740
Apples	2,265	2.2	4,983
Peas	566	8	4,528
Stringbeans	538	2.2	1,184
Onions (corrected)	680	2.7	1,836
Cabbage	2,265	4	9,060
Carrots	663	3.7	2,433
Tomatoes	1,614	2.6	4,316
Spinach	453	2.4	1,087
Beets	217	2.4	521
Navy beans	226	20	4,520
Potatoes (corrected)	8,154	3.8	26,185
Eggs	565	5.6	3,164
Neckbones	1,241	5	6,205
Bacon	226	11	2,486
Chopped meat	906	5	4,530
Veal	1,132	5	5,660
Kidney	906	10	9,060
Sugar (corrected)	1,586	0	0
Sugar, brown	453	0	0
Whole wheat cereal	725	20	14,500
Farina	906	3	2,718
Rolled oats	906	22	20,532
Rice	1,359	1.6	2,174
Flour	906	3	2,718
Apple butter	226	1.2	271
Cocoa, coffee, vinegar, etc.	......	0	0
Total vitamin		(week) 237,989	
		(per day) 33,998	
Total calories (calculated by Spohn)		(per day) 12,599	
Vitamin/Calorie Ratio		2.70	
Body weight for which this value of the ratio is just adequate		95 kgm.	
Weight taken as representative of family		66 kgm.	

* *Family:* Father, mother, boy 15 years, girl 13, boy 4, girl 2 years. (Data covered period April 5 to April 12, 1932, and were obtained through courtesy of Dr. Adelaide Spohn.)

protein, calcium, phosphorus, iron, and vitamins as expressed in current standards for these dietary factors. The calculation of vitamin B content acquires special interest in this case, because the choices of food were made following the advice of a trained nutritionist; it affords an illustration of how a student of nutrition can solve the problem of securing an adequate ration at very low cost. The data pertinent to our calculations are shown in Table 74.

From Table 74 it appears that this family ate a diet having a VIT/CAL value of 2.70, which is almost identical with that for the average American diet as described by Sherman (see pp. 186). A large factor of safety against beriberi was thus obtained. In view of the fact that trained nutritionists in the United States follow essentially the same principles as were applied by Dr. Spohn in this family, it is reasonable to assume that the same results would be obtained in other localities where the advice of dietitians and others skilled in the science of nutrition is followed.

Representative Daily Diets of Children in the Mooseheart, Illinois, Children's Home

THROUGH the courtesy of Dr. Lydia Roberts and her associate, Ruth Blair, at the University of Chicago, food-intake data have been obtained, for representative days, of children living in six individual cottages at the Mooseheart Illinois Orphanage, an institution founded by the Loyal Order of the Moose. Similar data were also furnished for a girl living in a private home. The diets in use at this institution were planned and supervised by trained dietitians, and presumably, therefore, were of excellent quality.

A summary of the data pertaining to the calculations of vitamin B content is presented in Table 75.

The figures in the last column of the table indicate that the rations furnished a great abundance of vitamin B. The values of the VIT/CAL ratio are much greater in every case than that for the average American diet previously discussed (see page 186). It is quite possible that the vitamin B requirement of these children is somewhat greater than the value indicated by Chart 6 (p. 110), based on body weight and caloric requirement. Even if this be granted, and a higher value of the ratio be taken as representing the true minimum of vitamin intake, our prediction value would have

to be multipled by from about 3 to as much as 8 in order to reach the values shown in the last column of Table 75. It is reasonable, therefore, to believe that these children received a very liberal supply of vitamin B.

TABLE 75

*The Vitamin B Intake, on Representative Days, of Individual Children in Six Different Cottages at Mooseheart, Illinois, and a Child Living in a Private Home**

CHILD	AGE	WEIGHT	HEIGHT	VITAMIN B PER DAY	CALORIES PER DAY	VIT/CAL RATIO
	years	*kgm.*	*cm.*	*mgm.-eq.*		
Ernest C.	8	25.7	126.4	7,938	2,450	3.24
Dora F.	8	27.0	126.0	7,566	2,201	3.44
Catherine M.	6	20.6	107.5	4,642	1,213	3.83
Jack S.	4	15.5	98.5	5,044	1,326	3.80
Robert C.	7	23.1	117.6	7,542	1,996	3.78
Margaret E.	8	31.5	137.2	7,846	2,533	3.10
A. D. (girl) in private home	5	27.4	118.1	6,277	1,975	3.18

* The data, upon which these estimations are based, were kindly furnished by Professor Lydia J. Roberts and Ruth Blair of the University of Chicago.

Representative Diets Selected by American Women During Pregnancy

Coons (1933) has made dietary studies on women during pregnancy with the view to determining the adequacy of the diets voluntarily selected. In her study data from a total of 48 observation periods covering 212 days of pregnancy in 15 women were obtained. Group 1 included eight subjects living in Chicago, 1927–29; Group 2 consisted of women living in Oklahoma, 1931–32. "Eight of the subjects were primiparae, 4 secundiparae, one a tripara, and one a quadripara. The period of gestation was normal in most cases, with a tendency to prolonged gestation in the northern group."

Dr. Coons kindly furnished representative detailed data as to the foods ingested by six of the women, three from each group. When asking for the data we suggested that instances of what seemed to be *good* diets and definitely *inferior* food selections be chosen. The foods lists submitted by Dr. Coons have been examined for vitamin B content by the method already described, with the results shown in Table 76, fourth column from the right; these should be compared with the figures in the next to the last column, which indicate the estimated required value of the VIT/CAL ratio based on the cor-

rected body weight. The corrected value of the weight was obtained by adding together the initial maternal weight, that of the newborn infant and a reasonable allowance for the placental tissues. In this way an attempt was made to correct for the allantoic fluid which obviously can hardly be regarded as active tissue requiring vitamin B for its metabolism.

It is evident that in two cases—D of Group 1, and VI of Group 2—there was a very large factor of safety against beriberi. The ratios of the values yielded by the diet to those expressing the

TABLE 76

*The Vitamin B Contents of Diets Selected by American Women During Pregnancy**

CASE	PARITY	AGE	LACTATION	BODY WEIGHT			VITAMIN/CALORIE RATIO			
								Needed for Body Weights		
				Initial	Final	Final corr.†	Yielded by diet	Initial	Final	Final corr.
		years		*kgm.*	*kgm.*	*kgm.*				
Group 1										
C	II	24	++++	58.0		61.0	1.91	1.64		1.73
D	I	26	++	63.5	74.5	66.9	2.90	1.80	2.10	1.90
G	IV	35	++++	53.1	61.2	57.4	1.97	1.50	1.72	1.62
Group 2										
IV	III	31	++++	84.8	91.6	88.7	2.53	2.40	2.60	2.50
V	I	21	+	54.4	65.3	58.4	1.82	1.56	1.82	1.64
VI	I	23	++++	50.3	57.0	53.9	2.59	1.42	1.62	1.53

* The detailed data, upon which these estimations are based, were kindly furnished by Dr. Callie M. Coons.

† Corrected by adding initial maternal weight, weight of the infant, and 0.25 kgm. for placental tissues.

estimated need, based on the corrected body weights (last column) are 1.57 and 1.69 respectively. For case IV, the diet furnished just the amount required, judging from the value 1.01. The remaining cases had a factor of safety of from 10 to 22 percent.

It is quite possible that the true factors of safety are greater than these data indicate. If corrections for the body weight were to be made, based on the facts that women generally have more fat in their tissues than men, and that during pregnancy there is generally a tendency toward edema, then the corrected body weights to use in estimating the vitamin requirement would be appreciably less than the figures given in Table 76; this would operate to increase

the value of the ratios shown in the last column and therefore the factor of safety against physiological shortage of vitamin B. Whether such corrections of body weight should be made is doubtless one of the questions that must be left for further research to determine.

So far as I have been able to ascertain, there is a rather widespread opinion among American physicians and students of nutrition, that the average American woman receives ample amounts of vitamin B during pregnancy and lactation. If the women subsist on diets essentially like the one described previously as the "average American diet," then this belief is probably correct; that the diets may yield much less vitamin B is amply demonstrated by the data in Table 76. It seems pertinent to point out the fact that certain beliefs as to what is or is not desirable as a food for a woman during pregnancy and lactation have gained considerable currency, and these require special scrutiny from the standpoint of the thesis discussed in this monograph. Many of these ideas represent the views of clinicians who seek to combat a tendency toward edema or other undesirable conditions. Examination of the actual dietaries of pregnant women, who are being fed in accordance with the dicta of clinicians, should yield findings of interest in relation to this question, and constitutes another valuable program of further research.

Steffansson-Anderson "Exclusive-Meat" Diet

As a result of his experiences in the Arctic regions Steffansson has championed an exclusive-meat diet. A careful study of effects of such a ration on kidney function, blood composition, and other physiological categories of interest, was made by a group of investigators (McClellan and DuBois, 1930). In the course of this study Steffansson and his associate Anderson subsisted on a dietary made up entirely of animal tissue for over a year. "No clinical evidence of vitamin deficiency was noted." Inasmuch as a year of subsistence on a diet appreciably deficient in vitamin B would undoubtedly result in beriberi, and the disease did not appear in this experiment, an adequate supply of vitamin B was furnished by the diet. An estimation of the amount by our method has therefore been made. The results are shown in Table 77.

The value of the VIT/CAL ratio as given in Table 77 is less than the true value, because the caloric content of the marrow was included in the total calories furnished by the diet but the vitamin content was omitted, no assays for this tissue being available; likewise the vitamin-sparing action of fat is ignored. It will be noted that even when the calculation is made in this way, the high value of the 2.77 is obtained for the VIT/CAL ratio. From this result it is evident that Steffansson and Anderson should not have developed beriberi during the year of subsistence on an "exclusive meat" diet; the ration furnished liberal amounts of vitamin B and thus afforded a large factor of safety against the disease. These findings constitute another confirmation of the author's thesis.

TABLE 77

Vitamin B Intake of Steffansson and Anderson Who Ate an "Exclusive Meat Diet" for a Period of One Year

(Data of McClellan and DuBois, 1930)

FOOD	AMOUNT PER MAN PER DAY	VITAMIN INDEX	VITAMIN CONTENT	CALORIC INDEX	CALORIE CONTENT
	grams		*mgm.-eq.*		
Lean beef	390	5	1,950	2.0	780
Fatty tissue	175	?	0	7.8	1,365
Liver	200	32	6,400	1.29	258
Marrow	70	?	?	8.71	610
Totals			8,350	....	3,013
Vitamin/Calorie Ratio				2.77	
Body weights: of Steffansson				69 kgm.	
of Anderson				58 kgm.	
Values of Vitamin/Calorie Ratios required:					
For man of Steffansson's weight				1.96	
For man of Anderson's weight				1.62	

Average Dietary of Northern China

Adolph (1925), in a study of North China dietaries, collected data concerning the foods eaten by 340 adults and 114 children below 12 years of age, corresponding to a total of 19,777 adult unit days. From the tables which he published it has been possible to determine the composition of what might be called the average diet for the inhabitants of northern China. A study of the vitamin B con-

TABLE 78

Vitamin B Content of an Average North China Dietary

(Data of Adolph, 1925)

The data given below were calculated as "amounts per capita per day" from the data contained in Tables 1 and 3 of Adolph's paper.

FOOD	AMOUNT PER DAY	VITAMIN INDEX	VITAMIN CONTENT	CALORIC INDEX	CALORIE CONTENT
	grams		*mgm.-eq.*		
Meat, Fish and Eggs:					
Pork	11.7	30	351	3.0	35
Eggs	10.5	5.6	59	1.48	16
Fish	6.9	4.5	31	1.0	7
Shrimp and shellfish	5.2	2 (?)	10	1.11	6
Beef, mutton and mule meat	1.6	5	8	2.00	3
Legumes (figured as)					
Soy bean	34	23	782	4.33	147
Vegetables and Fruits:					
Green vegetables (33)	58	3	174	0.45	26
Cabbage	25	4	100	0.32	8
Leeks	13	10	130	0.33	4
Onions	7	2.7	19	0.49	3
Turnips, taro, etc.	4	4 (?)	16	0.50	2
Fruits (12 varieties)	4	2 (?)	8	0.40 (?)	2
Garlic	3	3	9	0.49	1
Celery	2	2.4	5	0.19	0
Sweet potatoes	1	3	3	1.23	1
White potatoes	0.8	3.8	3	0.97	1
Cereals:					
Wheat and wheat products	330	3	990	3.0 (?)	990
Rice	187	1.6	299	3.51	656
Millet	47	26	1,222	3.45	162
Kaoliang (sorghum)	30	20	600	3.45	104
Corn	8	20	160	1.01	8
Nuts:					
Chestnuts	3	22	66	4.03	12
Peanuts	3	40	120	5.48	16
Milk:					
Goat's and cow's milk	6	3.6	22	0.69	4
Miscellaneous:					
Butter and fat (chiefly oil)	42	2 (?)	84	8	336
Sugar and starch	18	0	0	4	72
Totals			5,271		2,622 (Adolph) 2,471

Vitamin/Calorie ratio	2.01
Body weight for which this value of the ratio is just adequate	71 kgm.
Average weight of adult male Chinese given as	55 kgm.

tent of such a diet is of particular interest here because beriberi is quite rare in Northern China in contrast to the southern part where it is of quite common occurrence. The foods entering into this aver-

age ration and the details of the calculations for vitamin B content are presented in Table 78.

Comparison of this Chinese diet with the average American diet (see Table 69, p. 186) reveals that the people of northern China eat much less meat, extremely small quantities of milk and dairy products, and considerably greater amounts of cereals, notably wheat, than do the inhabitants of the United States. As is well known, the soy bean, with its interesting edible by-products, constitutes a valuable component of the Chinese diet, and is relatively unknown in America.

According to Table 78, this average diet of the Northern Chinese affords a moderate factor of safety against beriberi. The VIT/CAL ratio has the value 2.01, which, according to Chart 6 (p. 110), is estimated to be just adequate for a body weight of 71 kgm.; the average weight of the male Chinese adult is given by Adolph as 55 kgm. The factor of safety against shortage of vitamin B in the case of this diet is appreciably below that of the average American diet; this is in accord with the facts concerning the incidence of beriberi in the respective countries, and therefore supports the author's thesis.

Rations Allowed by the German Government for the Civilian Population During the Winter of 1916–1917

In spite of the serious food shortage which occurred in Germany during the Great War, it is a fact that beriberi was absent. The literature dealing with the effects of this lack of nutrients on the health of the German people does not record the appearance of beriberi. This is rather astonishing and deserves serious study. Lusk (1921), in his review of the physiological effects of undernutrition, which dealt chiefly with observations made in the Central Empires during the war, cited a table from a paper by Rubner showing what the German government *planned* to provide as a daily ration for the civilian population and what was *actually furnished* during the winter of 1916–1917. These data have been examined for vitamin B content by our method. The results are shown in Table 79.

Following examination of the foods listed in Table 79 it will be readily appreciated that the estimation of vitamin B content can

be only roughly approximate. It is necessary to assume an average vitamin index value for the cereals, the "butter and margarine" and the meat items. If pork was used at all, the value of the index for the meats would be greater than that taken, namely 5. The fact that much of the slightly milled cereal products was used during the war would seem to justify use of the value 10 as the proper in-

TABLE 79

Vitamin B Content of the Food Supplies for the Civilian Population of Germany During the Winter of 1916–1917

"The department of food supplies of the German government planned to provide rationed foods in amounts which may be contrasted with the quantities actually furnished, as follows:" (Lusk, 1921—Rubner, 1918).

DIETARY COMPONENT	VITAMIN INDEX	AS PLANNED			AS ACTUALLY PROVIDED		
		Amount daily	Vitamin content	Calories, approximately	Amount daily	Vitamin content	Calories, approximately
		grams	*mgm.-eq.*		*grams*	*mgm.-eq.*	
Bread	2	271	542	688	271	542	688
Potatoes	3.8	710	2,698	710	357	1,357	341
Butter and margarine	8	18	144	140	11.4	91	89
Milk	3.6	200 cc.	720	111	.....	.....	.....
Meat	5	70	350	158	36	180	78
Eggs	5.5	35	204	53	9	54	13
Sugar	0	32	0	125	26	0	104
Cereals	10*	...	.....	.....	9.8	98	31
Totals			4,658	1,985		2,322	1,344
Vitamin/Calorie ratio		2.35			1.73		
Average body weight		60 kgm.			49 kgm.		
VIT/CAL value required by this weight		1.70			1.40		

* Assuming only slight milling of the grain.

dex for cereals in this calculation. Butter has an "index" of 8–10. If it be assumed that not more than one-fifth of the "butter and margarine" was butter, then an index value of about 2 would be the correct one to use for this item.

It appears that the ration as planned had a VIT/CAL value of 2.35, which indicates a moderate factor of safety against shortage of vitamin B. The people lost considerable weight, due to the fail-

ure to provide sufficient calories, the average body weight decreasing from 60 to 49 kgm. The VIT/CAL ratio of the ration actually provided was considerably less than that of the diet planned, but was still somewhat greater than that estimated to have been the absolute minimum. This finding would seem, therefore, to explain the fact that, although food was scarce, and undernutrition was very widespread, beriberi was not observed.

Diets of War Prisoners in Germany Before and During the Period of Food Stringency

Taylor (1917) was able to obtain data concerning the amounts of various foods eaten by war prisoners in Germany prior to and during the period of stringency in foodstuffs. These data are of interest in the present connection because beriberi has not been recorded as occurring in these prison camps. Taylor's food lists are presented in Table 80 together with our calculations of vitamin B content. Where it has been necessary to make any assumptions upon which to base an index value, this has been indicated. For example, "meat" is assumed to be beef, and therefore an index of 5 is taken; if pork was eaten at all, obviously the correct index value would be greater than 5. Since we are particularly interested in learning the smallest amount of vitamin that the diet could have contained, the value 5 is justified. All sausage is assumed to be beef. The nutrient yeast is considered to have been bakery yeast, which is appreciably lower in vitamin content than the brewery product. If the latter was used, then the vitamin content of the ration was greater than the calculation reveals, certainly not lower. Considerable difficulty was experienced in deciding what would be the appropriate index to use for bread, especially for that eaten during the period of food stringency. Taylor gives a brief description of it. Obviously it must have contained much bran and other material which is normally rejected in milling grain for human consumption. The three figures for vitamin content of this bread are those obtained when the vitamin index is taken as 2, 6 and 11, respectively. The lowest value, namely 2, applies to bread made with highly milled wheat flour and therefore represents a limit below which the correct index value for this war bread certainly could not have gone; whether the value should be as high as 11, which is approximately one half that for the

TABLE 80

Vitamin B Content of the Diet of War Prisoners in Germany Before and During the Period of Food Stringency

(Data of Taylor*)

FOOD	VITAMIN INDEX	CALORIC INDEX	PERIOD					
			Prior to food stringency			Of food stringency		
			Amount per day per man	Vitamin content	Calorie content	Amount per day per man	Vitamin content	Calorie content
			grams	*mgm.-eq.*		*grams*	*mgm.-eq.*	
Bread	2	2.50	300	600	750	300	600 1,800 † 3,300	750
Flour	3	3.53	40	120	141	7	21	25
Meat (beef)	5	2.00	43	215	86	29	145	58
Fish	4.5	1.00	43	194	43	46	207	46
Herring	4.5	1.42	21	95	30	0	0	0
Potatoes	3.8	0.97	1,286	4,887	1,247	500	1,900	485
Vegetables	3	0.45	257	771	116	236	708	106
Skim milk	2.6	0.37	57	148	21	71	184	26
Sausage (as beef)	5	2.00	29	145	58	29	145	58
Cheese	2	4.17	14	28	58	14	28	58
Nutrient yeast	60	2.00	5.7	342	11	2.9	174	6
Sugar	0	4.00	29	0	116	19	0	76
Legumes	10	3.55	21	210	75	21	210	75
Fat	0	9.00	10	0	90	9	0	81
Maize grease	0	9.00	26	0	234	14	0	126
Pearl barley	3	3.55	14	42	50	9	27	32
Dried Fruit	6	2.80	7	42	20	43	258	120
Marmalade	0	3.13	14	0	44	14	0	44
Tea	0	0	2	0	0	0.5	0	0
Coffee	0	0	0	0	0	0.8	0	0
Chicory	0	0	0	0	0	2	0	0
Spices, herbs	0	0	4	0	0	3	0	0
Cocoa	0	4.97	6	0	30	6	0	30
Mustard	0	0	0	0	0	7	0	0
Totals				7,839	3,220 (Taylor 2,740)		4,607 5,807 7,307	2,202 (Taylor 1,720)
Vitamin/Calorie Ratio				2.43			2.09 2.64 3.32	
Body weights for which values of ratio are just adequate				86 kgm.			74 kgm. 93 117	
Probable average body weights of prisoners				66 kgm.			50 kgm. 55	

* A. Taylor—The Diet of Prisoners of War in Germany, Jour. Am. Med. Assoc., 69: 1575–82 (November 10, 1917). The data in Taylor's Tables 1 and 2 (p. 1582) were changed from "amount per *week* per man" to "amount per *day* per man."

† The three figures given are those obtained when index values of 2, 6, and 11, respectively, are taken for bread.

whole unmilled grain, may doubtless be questioned. In all probability the true value to use for these estimations lies between these extremes.

From the data in Table 80 it appears that at no time should beriberi have appeared in these prison camps. *This agrees with the facts*, so far as they are recorded in the literature. In the period prior to marked shortage of food, the diet provided sufficient vitamin B for body weights up to 86 kgm. whereas the average weight of the prisoners, based on the studies of Davenport and Love (1921) of the United States draft troops, was probably about 66 kgm. The VIT/CAL value of 2.43 given in Table 80 is based upon the caloric content obtained when the caloric index values given in Table 21 are used. If Taylor's own figures for caloric content are taken, namely, 2,740 calories per day, the value of the ratio becomes even greater. For the purpose of the present study, where many diets are compared, the caloric content based on our caloric index values seems to be the proper one to take. These same considerations also apply to the calculations for the period of food stringency.

During the time when the food shortage became acute it appears that, although the daily ration provided approximately 1000 fewer calories, as a result of which the prisoners lost considerable weight, the VIT/CAL ratio was in all probability even greater than before; it was certainly adequate for body weights as low as 74 kgm., and probably was sufficient for weights up to as high as 93 kilos. From the fact that nutrient yeast was provided, it is evident that the authorities made some attempts to provide sufficient vitamin B; the chief difficulty encountered seems to have been with respect to the supply of energy, this resulting from the fact that the actual supply of all nutrients was exceedingly limited. The findings that the vitamin B contents of these rations were appreciably greater than the estimated minimum requirement, and that beriberi did not occur among these war prisoners, are obviously in harmony with our thesis.

Diets of Workers on Sugar and Cacao Plantations in East and West Indies

Seagar (1930) has collected data concerning the average daily intake of various foods by laborers on sugar and cacao estates in the

East and West Indies, and has endeavored to correlate these diets with the incidence of various disorders. The new method for estimating the vitamin B content of diets has been applied to these data with the results summarized in Table 81.

It appears that with respect to the sugar plantations in both the East and West Indies there is little difference in vitamin B content, and the amount of vitamin furnished by these diets must be regarded as only barely sufficient, or borderline; certainly the factor of safety against beriberi is quite small. The body weights for which these diets are just adequate lie between the extremes of weights characteristic for the laborers in question. In the case of the cacao

TABLE 81

Vitamin B Content of Diets Used by Workers on Sugar and Cacao Estates in East and West Indies

(Data of Seagar, 1930)

ESTATES	LOCALITY	VITAMIN/CALORIE RATIO	BODY WEIGHT	
			For which this value of the ratio is just adequate	Probable actual average weight
			kgm.	*kgm.*
Sugar	East Indies	1.38	49	40–56
	West Indies	1.36	38	40–56
Cacao	East Indies	1.21	45	40–56
	West Indies	1.58	56	40–56

estates in the West Indies, the vitamin B supply appears to be somewhat better; the body weight for which the available vitamin is just sufficient proves to be the probable upper limit of weights of the men.

These findings are particularly interesting because they accord well with what is known concerning the prevalence of beriberi in these localities. In his list of disorders to which these laborers were subject Seagar does not mention beriberi. Evidently, over the period covered by his statistics this disease was not observed. On the other hand many of the cases of beriberi reported by Bentley (1893) and others in the Far East appeared among the coolies on various plantations; and the incidence of beriberi in Java, Malay States, and neighboring localities has always been great enough to

warrant the statement, often made, that the disease is endemic in these regions. A fair conclusion to draw from these facts seems to be, that the diets used by a very large part of the population in the East Indies and in South America are very close to the borderline with respect to satisfying the need for vitamin B. The fact that our method of analysis, applied to data such as Seagar has collected, points to the same conclusion may be interpreted as constituting further evidence of the validity of the method.

Summary of Vitamin B Contents of Various "Good" Diets

In this chapter have been presented the results of examination of various diets use of which was not found to be associated with the disease beriberi. Calculations for vitamin B contents of these rations have uniformly revealed that they supplied adequate amounts of this important dietary factor, and therefore beriberi should not have developed. The factor of safety against physiological shortage of the vitamin in these "good" diets was found to vary somewhat. The average American diet furnishes quite liberal amounts of vitamin B, being superior in this respect to the average dietary in use in Northern China. The vitamin B content of the dietaries selected by American women during pregnancy, as recorded by Coons, showed rather marked variations, the amount in some instances being rather close to the estimated minimum, others being much higher and approximating that of the average American diet. The indications from this work are that further more extensive observations should be made.

It is interesting to observe that the diets available to the civilian population of Germany during the Great War, and the rations in use in the German camps for war prisoners, furnished sufficient amounts of vitamin B, even when there was a serious lack of food and widespread under-nutrition (calorie shortage) prevailed. This finding accords well with the facts concerning the absence of beriberi. Likewise, the subsistence of Steffansson and Anderson for a year on an extreme diet consisting exclusively of "meat" without the appearance of beriberi is readily explained by the finding that this ration, subjected to our method of analysis, furnished a liberal amount of vitamin B.

CHAPTER XIV

INTERESTING FACTS RELATING TO BERIBERI: THEIR EXPLANATION IN THE LIGHT OF THIS INVESTIGATION

THERE are several interesting facts relating to beriberi which students of this disease have attempted to explain. In this chapter these are examined in the light of the results of this investigation.

Sex Incidence of Beriberi

Students of the beriberi problem have frequently commented on the fact that this disorder is preëminently a disease of young adult males. As an explanation of this it has been suggested that beriberi is chiefly an "institutional disease," that is to say, a disorder found in jails, asylums, groups of laborers and the like, and that the conditions in society which operate to form these groups affect men more than women. The results of the present study suggest another explanation. The formula derived from these quantitative studies indicates that the two most important variables determining the vitamin B requirement are the body weight and the metabolism. The exact meaning of this factor called metabolism may not be entirely understood at the present time; it seems obvious, from our dietary studies, however, that the calories representing the total energy exchange per unit of time may be taken as a rough measure of it. Now it is generally known that males have a distinctly higher rate of metabolism than females, and being usually heavier and more active, consequently consume greater quantities of food. Therefore, males have a higher total energy exchange per day. Under conditions where the vitamin B content of the ration proves to be very close to that required by the organism, there is little or no factor of safety against beriberi, and this sex difference in total metabolism may be the chief factor determining whether beriberi shall develop. Under such circumstances it is obvious that the males should be more liable to the disease.

The clinical literature indicates that women are more suceptible to beriberi during pregnancy and lactation. The observations of Hoffman (1924) may be cited in this connection as well as the earlier literature summarized in Vedder's (1913) monograph. Studies of the metabolism during pregnancy (DuBois, 1924), indicate that there is indeed an increase in the basal rate and this is accounted for by the metabolism of the growing fetus. If, then, a woman is subsisting on a diet which is borderline with respect to adequacy of vitamin B, and she escapes beriberi when in the non-gravid state, she may nevertheless become susceptible to the disease during pregnancy. The most important determining variable here would seem to be the magnitude of the factor of safety afforded by the dietary.

The Age Factor in Beriberi

As has already been pointed out, beriberi is most common among young adult males. The breast-fed infant is next in order of susceptibility. The incidence of the disease among women is less, and among the elderly and the aged beriberi is comparatively rare.

With respect to the incidence of beriberi among infants several pertinent comments may be made. The most recent elaborate discussion of infantile beriberi seems to be that of Ohta (1930) based on observations made in the clinics of Tokyo. 414 out of 430 cases, or 96 percent, were breast-fed. Boy babies are affected more readily than girls. Similar observations have been reported by other investigators (see Vedder's review). As stated previously, this sex difference may be attributed to the higher rate of metabolism characteristic of the male. The high incidence of infantile beriberi among rice-eating people is doubtless related to three important facts: (*a*) During about the first six months of life the human infant subsists almost entirely on milk and therefore is in the group of individuals who live on a restricted dietary; (*b*) it has been shown that the amount of vitamin B present in the milk depends primarily on the quantity ingested by the mother (Sure, 1928; Evans and Burr, 1928); (*c*) most of the diets in common use throughout the Far East, where so many cases of infantile beriberi occur, are deficient or just barely adequate with respect to content of vitamin B, and therefore the amount of the ingested vitamin available for passage

through the mammary gland is small, and as a consequence the milk is deficient. It has been estimated by Sure, (1928) and by Evans and Burr, (1928) that a lactating rat requires from three to five times more vitamin B in order to nurse a litter of young successfully than she needs for the maintenance of her own organism.

One may well inquire why the incidence of beriberi in children between the weaning age and puberty is so low. The following explanation based on this investigation is offered. When a child is weaned it begins to eat foods that are more concentrated with respect to energy, protein, and other factors, than milk. Let us refer to the plot of our formula for estimating the vitamin B requirement (see Chart 6, p. 110) and consider its implications. Notice the dotted extension to the left of the plotted line A of Chart 6. Now this line represents the plot of the VIT/CAL ratio as ordinate against BODY WEIGHT as the abscissa. The slant of the line indicates that for the smaller weights characteristic of children the values of the VIT/CAL ratio are much less than those for adults. For example, a diet with a VIT/CAL value of 1 would be just adequate for adults weighing approximately 36 kgm., in contrast to minimum values of from 0.25 to 0.85 for body weights ranging from 10 to 30 kilos, the range covering weights of children. It may be argued that during growth there is a greater requirement for vitamin B. This may be freely admitted without in any way affecting the argument, because the measurements upon which the formula is based take account of the growth factor. From this it is clear that a diet with a VIT/CAL value of only 0.68, for example, which is so low as to permit an epidemic of beriberi among the adult males in the Singapore Prison in 1875 (see Table 35, p. 134) could still be adequate for young children; they would not incur beriberi if restricted to such a ration. As the children increase in size the value of the VIT/CAL ratio required by the individual increases; and, in those regions where beriberi is endemic due to the average dietary furnishing too small a factor of safety against beriberi, the value of the ratio increases until it approximates that characteristic of the diet, and the individuals now join the adult group for which the vitamin supply is barely if at all adequate, and whose susceptibility to beriberi is consequently very great.

Association of Beriberi with Malaria and Other Fevers

The clinical literature contains numerous reports of the occurrence of beriberi following prolonged fevers. Such an association has led some clinicians to adopt the view that beriberi is after all an infection and not a vitamin B deficiency.

Bentley (1893) described 52 cases of beriberi, 28 of which appear to have been the sequel of recurring malaria or dysentery and allied conditions. These cases were observed in Java. If the diets in common use in Java at that time were at all like those employed in the prisons as described by Vordermann (see Table 40, p. 143) then they were borderline with respect to adequacy of vitamin B. Three cases of beriberi following relapsing fever were reported by Yacoub (1918), and in each instance there was prolonged feeding of condensed milk, a food containing liberal amounts of vitamin G but relatively small quantities of the B factor. Walshe (1918) observed 40 cases of beriberi in Egypt, and of these, 19 percent showed a previous history of malaria. I have already referred to the contention of Cannon (1929) that the dry and dysenteric forms of beriberi are really camouflaged forms of malaria (see Chapter II, p. 7) and the views of several Brazilian clinicians that beriberi as seen in their country must be an infection instead of a dietary deficiency.

Let us consider the matter in the light of the vitamin formula that has come out of this research. In malaria, as in fevers, there is a heightened metabolism (DuBois, 1924), and therefore one should expect to find in these conditions an increased requirement for vitamin B. If the malaria patient were to remain in bed, thus reducing to a minimum the energy exchange due to muscular activity, there might be some slight compensation or saving of energy expenditure with which to offset the increase due to the chills and fever. In malaria, however, most patients are not bedridden sufficiently to obtain even this saving, with the result that the total energy exchange is significantly greater than that of the individual under normal conditions. Furthermore, malaria, unless properly treated, continues over a long period of time. If, now, such a condition obtains when the dietaries in common use are only borderline with respect to vitamin B adequacy, or furnish only a slight amount over and above that required daily, obviously a state of vitamin B

deficiency may readily develop. There is of course the additional theoretical possibility, that the metabolic responses of the organism to the presence of the malarial plasmodium in some unknown way affect the body's use of vitamin B and thus operate to increase the requirement for this dietary factor in a special and unique fashion. Future research alone can determine the correctness of such a hypothesis. How shall we explain the observation of Fraga, cited on page 16, that neoarsphenamin proved to be a valuable remedy in treating an epidemic of beriberi? Obviously, any therapy which is successful in eliminating the infection to which the *heightened* vitamin B requirement is due, operates in these cases also to cure the beriberi.

From these considerations, and in the absence of definite detailed dietary studies pointing to the contrary, one is certainly led to believe that beriberi in Brazil, as elsewhere, is due to lack of vitamin B, and that its frequent association with malaria is to be explained as due to the long-continued occurrence of a fever in patients subsisting on diets with low factors of safety against vitamin deficiency. In the absence of any quantitative evaluation of human diets for vitamin B content, and any fairly definite ideas as to what factors determine the organism's requirement for the vitamin, the clinical facts concerning this interesting relation of beriberi to malaria and other fevers would appear as strong evidence against the view that beriberi represents a dietary deficiency. In the light of the data submitted in this monograph, however, these facts find a reasonable explanation which is in harmony with the deficiency disease theory.

Frequent Association of Beriberi with Diarrheal Conditions

The frequency with which beriberi is associated with dysentery, ankylostomiasis, and other conditions characterized by more or less severe diarrhea, is a fact which impresses anyone who reads the clinical literature relating to this field. As with malaria the natural tendency has been to consider such cases as evidence against the view that beriberi is a deficiency disease. An equally tenable hypothesis would seem to be, that chronic or semi-chronic diarrhea can operate to cause a failure of the individual to absorb a sufficiently

large fraction of the ingested vitamin to meet the needs of the organism. This failure of absorption naturally would become more important as a contributory cause of beriberi when the amount of the vitamin in the diet is low or only barely sufficient, in which case the factor of safety against beriberi would be small even for the normal individual. The idea of Simpson (1920) that an excess of carbohydrates in the dietary contributes in some way to the development of beriberi, might be explained along the same lines. The studies made by McCay (1908) of the rations in common use in the jails of Bengal and Behar emphasized the association of a carbohydrate-rich dietary in man with the passage of numerous stools and the utilization of only from 40 to 60 percent of the ingested protein. It is not unreasonable to suppose that a similar failure of absorption of ingested vitamin B occurs with a food mixture in which carbohydrate forms an extremely large part. At the present time practically nothing is known concerning the locus of absorption of vitamin B in the intestine and the factors which influence this absorption. Observations of experimental animals in our own laboratory indicate that *simple* diarrhea does not cause the body to lose through the intestinal wall any of the vitamin already absorbed and stored in the tissues. The question as to whether it operates to diminish the absorption of ingested vitamin remains to be investigated fully. It is quite possible that the diarrheal conditions, which have appeared to be specially related to the incidence of beriberi, really were complicated by fever and an enhanced metabolism, and that the seemingly increased susceptibility to beriberi was due to this factor rather than the diarrhea.

CHAPTER XV

VITAMIN B IN RELATION TO OTHER CLINICAL CONDITIONS

IN addition to the facts concerning beriberi which have just been discussed there are many others which should be of interest to physicians, especially those in North America where manifest beriberi is comparatively rare. Inasmuch as vitamin B is classed by the student of nutrition in the group of substances absolutely necessary for the maintenance of growth and physiological well-being, and varying degrees of malnutrition are of common occurrence among the sick, the clinician should be particularly interested in making sure that the patient receives ample supply of this factor. A discussion of the possibilities in this field will now be presented.

When considering the application in the clinic of the experimental work of physiologists concerning this dietary essential it is advantageous to distinguish between the state of extreme deficiency, as seen in beriberi, and that in which there is only a moderate shortage of this vitamin. In beriberi the syndrome is quite well defined and this fact is of great aid to an accurate diagnosis. Quite a different state of affairs characterizes a moderate lack of vitamin B. In such cases the picture is not very clear-cut but rather confused, and in consequence there may be considerable difference of opinion regarding the significance or even the existence of various alleged features of the syndrome. Obviously, then, progress in this field must necessarily be slow, and every step forward must be taken with proper scientific caution; it is particularly important that an open-minded attitude with respect to developments in this field be preserved at all times.

For the clinician of North America the greatest significance attaching to vitamin B may be in its possible etiologic relation to various chronic conditions summarized in the vague term "ill-health." In these instances the shortage of the vitamin may not be great enough to result in manifest beriberi but sufficient to produce

a complication difficult to recognize and one which therefore escapes treatment.

Gastrointestinal Disorders

Reference has already been made to the possible rôle of diarrhea as a contributory cause of beriberi. There are other gastrointestinal conditions in which lack of vitamin B appears to play an important part.

It is conceivable that gastric achlorhydria favors the development of beriberi, particularly when the diet is restricted to a considerable extent. On the other hand, there is the possibility that the failure of the gastric glands to secrete acid is the result rather than the cause of a lack of vitamin B. Achlorhydria has been reported as occurring frequently in beriberi but not invariably (Ohta and Izumita, 1930). Minot (1929) had occasion to observe two cases of diabetes associated with peripheral neuritis and achylia gastrica "whose symptoms slowly improved upon taking large amounts of a concentrate of yeast," and made the interesting comment that "one must wonder if achylia gastrica is not a factor that can inhibit the utilization of both the P. P. (pellagra-preventive) and antineuritic factor of vitamin B." This condition described by Minot is by no means rare. Wohl (1926) observed an "avitaminosis in the course of diabetes . . . with symptoms and lesions of beriberi predominating." A case of "beriberi following drastic voluntary dietary restriction" as a result of stomach trouble was recently reported by Riesman and Davidson (1934). A similar case was also observed by Brauchle (1933). In both instances treatment with foods rich in vitamin B was followed by dramatic recovery. Cowgill and Gilman (1934) experimented with Pavlov gastric pouch dogs subsisting on artificial diets deficient in vitamin B and obtained results suggesting very strongly, although not proving absolutely, that a lack of this dietary factor can operate in some unknown way to depress the acid-secreting response of the gastric glands to appropriate stimuli. Confirmatory observations have also been reported by Webster and Armour (1934).

Gastric ulcer is another disorder which can conceivably be related to vitamin B deficiency. Insofar as the treatment of this condition usually involves a marked restriction of diet the occurrence

of at least a moderate shortage of this vitamin is by no means unlikely. Obviously the length of the period of dietary restriction is an important determining factor. Dalldorf and Kellogg (1931) observed in rats subsisting on carefully controlled diets that the incidence of gastric ulcer was greatly increased in vitamin B deficiency. Observations of this type merit serious consideration. The careful clinician will therefore give attention not merely to the treatment of the ulcer itself, but the maintenance of a satisfactory nutritive state as well, and this will involve the administration of vitamin B together with other important nutritive factors.

The question whether jaundice is related etiologically to beriberi has received some consideration. On the basis of his observations in a group of forty cases of beriberi Walshe (1918) gave a negative answer to this question. Two points of view may be taken here. One may regard the jaundice as a complication in no way related specifically to lack of vitamin B. One may also consider that the presence of jaundice is proof that alimentary functions are abnormal and these in turn may favor the development of vitamin B deficiency, especially when the diet is only barely adequate with respect to this factor.

Because of the high incidence of pathological changes in the intestinal mucosa in his experimental animals McCarrison (1920a) was led to believe that a liberal supply of vitamin B is very important in maintaining the health of the intestinal tract. Such a view is not without support from the clinical literature. A case of beriberi complicated by duodenal ulcer was described by Middleton (1914). In this instance it is possible that the presence of the ulcer acted to favor the appearance of beriberi by affecting the individual's eating habits and choices of food. The beriberi literature (see review by Shimazono, (1931) page 18) indicates that in human beings lack of vitamin B acts usually to depress the motility of the alimentary tract and constipation is of common occurrence. It is interesting, therefore, to see in Larimore's (1928) five cases of chronic ulcerative colitis instances where marked improvement and definite healing of the ulcers occurred accompanying the use of diets "rich in vitamins." Larimore expressed the opinion that "great excess of vitamin B is essential," and cites Grundzach (1924) as showing that chronic diarrhea may be related to a colitis caused

by lack of vitamin B. Such observations as these are very suggestive and indicate possibilities which should be carefully investigated. Trial of parenteral administration of vitamin B should be made in such cases as well as those of colectomy and related conditions characterized by more or less continuous diarrhea.

Heart Disorders

Consideration of this topic should be of interest to American clinicians. Students of beriberi have long recognized certain cardiac symptoms as important elements in the syndrome of this disease. Whether the prognosis is favorable or not depends largely on the prominence of the heart manifestations. The chief finding at autopsy is enlargement of the right side of the heart. Nagayo (1913) believed that this dilatation is due to fatty degeneration of the cardiac tissue and attributed the hypertrophy of the right chamber to congestion in the lungs. Reinhard (1916) used the X-ray in his studies and concluded that there is first of all a dilatation of the vessels, especially those of the pulmonary circulation, as well as of the right side of the heart. Reinhard was uncertain as to the exact cause of this and mentioned as possibilities degeneration of the vagi, phrenics or abdominal sympathetics. In view of the fact that the vascular symptoms, such as low blood pressure and bradycardia, showed improvement following injection of atropin, he favored the view that these phenomena are vagotonic in origin.

In 1910 Yamagiwa suggested that this cardiac enlargement results from the secretion of an increased amount of epinephrin and the effect of this on the entire circulatory system. This view is supported by the further work of Ohno (1922–23) and contradicted by the results of Matsumoto and Yoshimura (cited by Ohno), and therefore would seem to be still an open question. A similar situation prevails with respect to evidence from the field of animal experimentation, McCarrison (1920) interpreting his results with pigeons in terms of this hypothesis and Beznak (1923) failing to confirm this view.

The studies of Aalsmeer and Wenckebach (1929) support another explanation. These investigators champion the idea that the so-called hypertrophied heart characteristic of beriberi is really an edematous organ and explain the various vascular phenomena

on this basis. These authors believe that the fundamental process in beriberi is water retention and consequent swelling of certain vital tissues, especially the heart and striated muscle. In further support of this view one may cite the observations of Mebius (1929), who interpreted his pathological findings as indicating that in the beriberi heart water is bound in the anisotropic or contractile substance and not in the sarcoplasma. Mebius went so far as to suggest that the real function of vitamin B may be the control of osmotic conditions in contractile tissues, a generalization which is too broad, in my opinion. Aalsmeer and Wenckebach (1928) emphasize that the cardiac dilatation in vitamin B deficiency may be detected long before the first signs of polyneuritis. This observation should be of great significance to clinicians, particularly those specializing in cardiac disorders. The symptoms of interest here, according to Shimazono (1931), are a lowering of the diastolic blood pressure, audibility of the crural tone and the appearance of an epigastric pulsation. Aalsmeer (1931) cites a marked lowering of the minimal pressure and great difficulty in determining any fairly fixed value for it as important points in the differential diagnosis of the beriberi heart.

The effect of the administration of vitamin B on the heart in beriberi is striking. There is a rapid return of the heart to normal size, a fact which is definitely against the view that a true hypertrophy of the cardiac tissue occurs in beriberi. This diminution in the size of the organ is accompanied by a marked secretion of urine. Rigler (1928) studied the effects on the heart of the Jansen-Donath crystalline vitamin B and concluded that this substance might well be called a "heart automatin." The view that the heart in extreme vitamin B deficiency is an edematous organ finds further support in the data of Wassenmeyer (1930) who showed quite definitely that in the B-deficient bird the heart does contain more water than the organ of the normal individual.

Such observations as those just cited naturally have some bearing on the question as to the origin of the edema in wet beriberi. On the basis of his studies Yamaguchi (1928) concluded that this edema is largely extra-renal in origin. It is obvious that any marked impairment of the circulation such as would be expected from the beriberi heart might well contribute to the production of edema.

The fact that edema does not occur in all cases doubtless means that other factors play a rôle. Another well-recognized cause of edema is dietary in nature, and involves essentially a long continued subsistence on a dietary low in protein. The electrolyte content of the diet may also play a rôle. If one bears in mind the fact that the diets of human beings are quite variable and consequently may result in multiple as well as single deficiencies, one can formulate some basis for an explanation of the fact that certain cases show the "wet" or edema type of beriberi, whereas others exhibit the "dry" form. In a preliminary experiment with dogs subsisting on artificial diets Cowgill and Darrow (1933) were unable to produce a picture of vitamin B deficiency complicated by an edema. Further experiments are required on this problem.

Various Neurological Conditions

Pathological changes in the nervous system are found not only in beriberi but in many other disorders. Spinal cord lesions occur in advanced cases of pernicious anemia. Lesions in the brain have been described as characteristic of human pellagra. Lhermitte (1916) and Kimura (1919) claimed that, so far as the central nervous system is concerned, their histological preparations obtained from cases of human beriberi were indistinguishable from those of toxic polyneuritis, notably that due to ethyl alcohol. To what extent one is justified in assuming that a lack of vitamin B is involved in the production of these various lesions no one can say at the present time.

The fact that the development of pernicious anemia involves a long previous history of gastric abnormality combined with a dietary factor, according to Castle's (1929) theory, may be cited in favor of the view that in the pernicious anemia patient there has been ample opportunity for a vitamin B deficiency as well to develop. Fouts and associates (1932) observed six patients having pernicious anemia and one individual with carcinoma of the stomach, all of which showed long-standing involvement of the central nervous system. These patients received injections of vitamin B which were without influence on the neurological features of the syndrome. In all probability this negative effect is due to the lesions having been of an irreparable nature. These investigators re-

ported, however, that there was "an improvement in appetite, strength, and sense of well-being at the beginning of the therapy," which suggests very strongly that a shortage of vitamin B had contributed to the development of the lesions. Such experiments as these emphasize the importance of parenteral administration of vitamin B in treating clinical conditions.

The lesions of the central nervous system observed in human pellagra may or may not be due to lack of vitamin B. There is some evidence that a shortage of the G (B_2) factor may play an etiologic rôle here (Zimmerman, Fox and Cowgill, 1934). The observations reported by Zimmerman, Cohen and Gildea (1934) on alcoholic pellagrins are worthy of comment here. One of these patients received a vitamin B concentrate parenterally and the first observation of note following the injections was a marked improvement in the condition of the tongue and the stomatitis; the second observation of interest was a return of the appetite to the patient who had previously been forcibly fed for a considerable period. This suggests that parenteral administration of vitamin B should be tried on cases of pellagra. If lack of this factor is involved in the production of the sore tongue and stomatitis, which in turn causes the patient to refuse food or to restrict himself to nutrients which are easy to swallow, then parenteral administration of vitamin B constitutes a therapeutic procedure of the first order of values, as a means of securing the patient's coöperation in eating an adequate diet.

A "gestational polyneuritis" believed to be due to lack of vitamin B has been described. Strauss and McDonald (1933) treated all of their three cases successfully with vitamin B. In this connection Plass and Mengert (1933) make the following comment:

> On the basis of the hypothesis that the disease results from a deficiency of vitamin B, intelligent prophylaxis would demand attention to secure an adequate consumption of this accessory food factor during and after hyperemesis gravidorum. With the recent tendency to force a high carbohydrate diet on patients with vomiting of pregnancy, there would seem to be an increased risk of producing vitamin deficiencies, unless special care is paid to inclusion of foods rich in these factors. Curative treatment is generally ineffective, unless one is impressed by the results of vitamin B feedings in the three cases of Strauss and McDonald (1933). It would appear that their cases were mild in character, but the record of 100 percent recoveries is impressive.

With extracts of vitamin B now available for parenteral administration it is not unlikely that the more severe cases can be treated successfully. This certainly merits clinical trial.

Anemias

I have already mentioned the trials of vitamin B therapy in cases of pernicious anemia by Fouts and associates (1932), who were particularly interested in the neurological features of this disease. There have been attempts to use this vitamin in the treatment of other anemias. The hypothesis underlying these studies has been that if certain anemias may be classified as deficiency diseases, then it is not unlikely that the dietary condition predisposing to the development of the anemia and operating over long periods may also lead to a physiological shortage not only of the factors required for functioning of the bone marrow but of other dietary essentials as well. From this point of view it is just as important to improve the anemic patient's general nutritive state as it is to treat the anemia itself. Rhoads (1933) and Minot (1931) emphasize the importance of this.

Davidson (1931) gave an autolysed yeast preparation as a source of vitamin B to patients exhibiting different types of anemia and secured favorable results in one instance. Fouts and associates (1932), who made injections of a vitamin B extract, "were unable to maintain the red blood cells of the patients (pernicious anemia) at their original level." In her studies of a tropical macrocytic anemia prevalent among the women of Bombay, India, Miss Wills (1931) found the English vitamin B preparation *marmite*, prepared from autolysed yeast, to be effective. According to her more recent report (1933), however, she finds that the effective agent in this preparation is neither vitamins B_1, B_2 nor B_4, and that large doses of dried yeast and water extracts of yeast are therapeutically inactive with respect to this particular anemia. The fact that whole yeast is ineffective whereas an autolysed product is of value emphasizes a very important point which all students in this field should bear in mind. Whole yeast, the autolysed material, and many other sources of vitamin B are really quite complicated mixtures. Because they have therapeutic value in relation to certain diseases and happen to be fairly rich in vitamin B content, it does

not necessarily follow that they owe their usefulness to their vitamin content. This is merely one possibility which, however, must be demonstrated by repeated trials with numerous extracts varying widely in composition and method of preparation but being similar in that all of them are very rich in content of the vitamin.

Infant Nutrition

In considering the incidence of beriberi as influenced by age infantile beriberi was discussed (see p. 209). The clinician in the United States may well ask himself whether this disease, because of its rarity, is worthy of serious consideration in relation to his practice. There are ample reports from the American clinical literature, however, indicating that the subject of the relation of vitamin B to infant nutrition under the conditions prevailing in this country possesses serious import. Moore and Brodie (1927) reported a case of hemorrhage in a new-born infant which gave evidence of beriberi. In this instance the mother's diet was markedly deficient in vitamin B. These authors, in commenting on this case, stated that "diets restricted by poverty, pernicious vomiting, diabetes and other causes need careful scrutiny from the standpoint of vitamins." Hoobler (1928) has described a syndrome observed in infants and believed to be indicative of lack of vitamin B. Important features of this clinical picture are anorexia, a strange plaintive cry and a more or less spastic condition of the arms, legs and neck. The administration of sufficient amounts of vitamin B results in prompt alleviation of these symptoms. Ohta (1930) cites Rehyer's description of a very similar condition and suggests that it represents infantile beriberi. This is borne out by the fact that vitamin B therapy proves to be effective.

Studies have been made of the amount of vitamin B in human milk and cow's milk and the findings correlated with the clinic. Outhouse, Macy, Graham, and Long (1927) assayed pooled human milk secured from individuals subsisting on what might be regarded as an average American diet, and came to the conclusion that this milk did not furnish an optimal amount of vitamin B for growth of the infant. Dennett (1929), Hoobler (1931), Bloxsom (1929), Waring (1929) and Haas (1929) have reported favorable trials of supplementary feedings of materials rich in vitamin B,

which serve to confirm the conclusion of Outhouse and associates. In view of these observations, and the fact that vitamin B is a dietary essential which should be present at all times in adequate amounts, and not a foreign substance similar in nature to a drug, the pediatrician has ample justification for the practice of supplementing the infant's diet with liberal amounts of vitamin B.

In the treatment of many marasmic infants who present evidence of dehydration it is a rather common practice to inject large volumes of fluid. It is quite possible that in certain cases this is really harmful unless vitamin B is given at the same time. In their study of dogs subsisting on vitamin B-deficient diets Stucky and Rose (1929) noticed the development of anhydremia. In other experiments with such animals, Cowgill, Rosenberg and Rogoff (1930) observed that the anorexia due to lack of vitamin B appears much sooner in animals given forced administration of large volumes of water sufficient to induce a vigorous diuresis; control dogs receiving liberal quantities of the vitamin maintained a perfect appetite while receiving similar administrations of water. When the B-deficient animals, in which anorexia had appeared, were given the missing vitamin, their urge to eat was restored promptly although the water administrations were being continued. If, now, the marasmic baby, who is being treated for an anhydremia, owes its condition in part to a lack of vitamin B, the administration of the usual therapeutic fluids may not yield the desired results; in fact, these water administrations may even be harmful, especially when they result in an appreciable diuresis, and presumably a washing out of more vitamin B. The proper procedure to follow would seem to be to add liberal amounts of a suitable vitamin B concentrate to the fluids given to marasmic infants. This suggestion is worthy of clinical trial.

Clinical Conditions of Heightened Metabolism

Reference has already been made to the fact that hyperthyroidism in experimental animals increases the vitamin B requirement (see Chapter VIII, p. 65). Such a finding suggests interesting clinical possibilities which should be investigated. The frequent occurrence of a sore tongue and other evidences of stomatitis in hyperthyroidic patients coupled with the observation of Zimmer-

man, Cohen and Gildea (1934) that vitamin B injections into a pellagra patient resulted in marked improvement in the condition of the tongue, suggests that in such cases of hyperthyroidism there is a serious shortage of vitamin B. In the light of the present investigation a state of vitamin B deficiency might readily be expected in persons with heightened metabolism due to overactivity of the thyroid gland.

It has become common practice to treat such a condition as typhoid fever with a high calorie diet in an endeavor to counteract loss in body weight due to consumption of the body itself in the prolonged fever. The results of the present study suggest that when so doing the clinician should take care to insure a liberal supply of vitamin B along with the additional calories.

These two illustrations will doubtless suggest to the thoughtful clinician other possibilities worthy of study.

Anorexia

The conditions discussed in the preceding sections all represent serious lack of vitamin B. When the shortage is only moderate, it is much more likely to escape notice and to be entirely unappreciated. Carefully controlled experiments on animals have demonstrated that anorexia is usually the first symptom to appear. For illustrations of such experiments on dogs the reader is referred to Chapter V, p. 40.

This anorexia should be of significance to the clinician, especially because it may occur in the absence of any other sign that the vitamin B supply is inadequate. Loss of the urge to eat is generally regarded not as a disease in itself but as a symptom, and this is doubtless the correct attitude to take. It is obvious that the loss of interest in food may be the result of many factors, some psychic and others associated with disease quite unrelated to vitamin B deficiency; it is not logical to assume that the administration of vitamin B in such cases will restore the urge to eat. Inasmuch as this procedure can do no harm, however, it would seem to be a wise one to adopt, if for no other reason than to rule out a lack of this vitamin as a possible cause of the anorexia in question.

There is ample clinical evidence already at hand showing that this anorexia does occur in the human species. Many of the trials of

vitamin therapy have been made on marasmic infants with favorable results. Hess (1917), Eddy and Roper (1917), Byfield and Daniels (1920), Bloxsom (1929), Waring (1929), Haas (1929), Hoobler (1928, 1931) and Dennett (1929) have reported on such tests in this country; Rehyer (1923) has obtained similar results in Europe. Newburgh was able to increase the voluntary daily food consumption of a young woman from about 400 to approximately 2,000 Calories by administering vitamin B. Swineford (1930) had occasion to observe a case diagnosed as mild beriberi resulting from a prolonged siege of typhoid fever and inadequate nutrition during convalescence. Administration of vitamin B brought about prompt correction of the anorexia and disappearance of the neuromuscular symptoms of beriberi. Anorexia is of common occurrence among the insane. Many of the epidemics of beriberi have occurred in insane asylums. It is frequently necessary to feed the inmates of such institutions forcibly for long periods. Vitamin B therapy with a view to restoring the urge to eat would seem to be especially worthy of trial in such instances. Even if only a small fraction of the number of such patients, or if only certain types of mental disorders were found to respond favorably to vitamin B administration, such results would be worth while. It is not unlikely that certain instances of anorexia in convalescents who have subsisted on hospital diets for long periods, and who have an unrecognized poor utilization of the ingested vitamin really represent a moderate shortage of vitamin B. Now that concentrates of the vitamin suitable for parenteral administration are available for clinical use, it becomes possible to investigate these possibilities and thus to learn the limitations of vitamin B therapy as well as its special fields of usefulness.

Restriction of Growth

As a result of the experiments of numerous students of nutrition considerable evidence has accumulated in support of the view that the various standards of growth of both experimental animals and man represent the growth that is possible under the dietary conditions prevailing. For example, one of the first standards for the growth of the rat was that offered by Donaldson (1915) based upon observations of the growth of a large number of rats fed a diet con-

sisting of milk-soaked bread with corn as a staple, and living under certain constant environmental conditions. When animals grew to the extent of about one gram per day over a selected period of reference, this growth was considered as satisfactory and conforming to the Donaldson standard. Later, by applying various discoveries concerning vitamins and other essential food factors, Osborne and Mendel (1926) were able to increase this rate of growth to about 3 grams per day. Further experiments resulted in a growth rate of 4 to 5 grams per day (Mendel and Cannon, 1927). The latest results are those reported by Anderson and Smith (1932) who secured the astonishing growth rate of 5.5 to 6.1 grams per day over the same age period of the rat's life. It should be borne in mind that these remarkable results were obtained with animals of the same genetic constitution, the colony having been inbred for many generations over a long period of years. It is difficult to escape the conclusion that the concentrations of the various dietary essentials, among them vitamin B, can play a very large rôle in determining the extent to which growth is possible.

Observations of this sort are not limited to experimental animals. There are indications of a similar change with respect to standards of growth in the human species. Formerly the conventional standard of growth of children was commonly expressed as "doubling of the body weight in six months and trebling in a year." More recently this has been changed to "doubling of the weight in three months and trebling in six months." In all probability this new standard results from the fact that the human infant growing in accordance with the old standard had its growth limited by a suboptimal supply of one or more of the dietary essentials. The conclusion of Outhouse, Macy and associates (1927), that the milk of many American mothers does not contain the optimal quantity of vitamin B, suggests that at least one of the dietary factors present in inadequate amounts is this vitamin. In the present discussion it should be borne in mind that we are considering not a shortage of the vitamin so great as to result in symptoms of beriberi, but a lack serious enough to evidence itself in some restriction of the normal growth process.

In their extensive monograph on nutrition McCollum and Simmonds (1929) have brought together considerable evidence show-

ing that the great majority of children, both in the United States and other countries, do not make the growth which one might reasonably expect in the light of the developments in the science of nutrition. In all probability many factors operate to bring this about, but there can be little doubt that the quality of the food and the quantity of the various dietary essentials furnished play important rôles. In dealing with individuals in the human species, who are able to choose foods within certain limitations, it is obviously exceedingly difficult to determine absolutely whether the limiting factor in most cases is a mineral nutrient such as calcium, or a vitamin, or some other essential factor. Morgan and Barry (1930) have endeavored to ascertain to what extent vitamin B is a limiting factor in the growth of school children who are markedly underweight. From their work it appears to be demonstrated that a shortage of this vitamin can be a factor in limiting the growth of American school children. Recent observations from our own laboratory (Dann and Cowgill, 1934) indicate that for growth young rats need from three to five times more vitamin B than the amount required for maintenance of the organism at any given body weight after having made excellent growth to that particular weight level. If these findings can be applied to the human species, then one may regard them as confirming the work of Morgan and Barry. Another finding of interest in the experiments of Dann and Cowgill relates to an apparent decided increase in the amount of vitamin B required at puberty. These observations were made on female rats. The lesson to be derived from all of these considerations seems to be that one should take care to provide more than enough vitamin B at all times both for the growing child and the adult.

Sources of Vitamin B for Clinical Use

Foods

Many clinicians consider that the problem of preventing and curing the conditions due to lack of vitamin B in the United States is readily solved simply by regulation of the diet. Alvarez (1931) may be cited as representative of this group. The results of the analyses of various American diets for vitamin B content, described in Chapter XIII, certainly lend much support to this view. The data concerning the incidence of manifest beriberi in the United States

may also be cited in favor of this position. On the other hand, sufficient clinical evidence has been cited in this chapter as well as in Chapters II and XIV to show that a lack of vitamin B may be a common complication encountered when dealing with other diseases, and in many of these clinical conditions the administration of this vitamin by mouth in the form of appropriate foods and crude concentrates may be quite ineffective in contrast to parenteral injection of the dietary essential.

The clinician should bear in mind that mere regulation of the diet operates to bring about a slow cure because it is almost impossible to supply huge quantities of the missing vitamin by means of the best of available foods. Shimazono (1931) expressed the view that many of the early failures of vitamin B therapy in beriberi were due to the administration of too small doses of the missing dietary factor. Numerous animal experiments have shown that the rapidity with which a cure is brought about is closely related to the quantity of the vitamin administered and the way in which it is given. The dog shown in Figures 7 and 8 is a good illustration of this. If relatively small but adequate amounts of vitamin B are given by mouth, there is a gradual improvement; parenteral administration of large doses is followed by remarkably prompt cures. It is reasonable to suppose that the rapidity of cure is related to the promptness with which a large amount of the vitamin reaches important tissues of the affected organism. Therefore, the procedure that should be recommended involves first of all the parenteral administration of vitamin B accompanied and followed by feeding of a vitamin B-rich diet. With respect to the foods that may be used in order to obtain an increased intake of the vitamin the reader is referred to Table 21 (p. 87 *et seq.*).

Special Concentrates of Vitamin B

THE preparation of such material suitable for clinical use constitutes an important biochemical problem. Most of the work concerning the preparation of vitamin B concentrates has had as its objective the isolation of the vitamin, and the procedures by which this has been done are so involved and costly that they are hardly practical upon any large commercial scale. Because of the wide prevalence of beriberi, the Bureau of Science in Manila, Philippine

FIG. 7

Dog Exhibiting Nervous and Muscular Symptoms of Vitamin B (B_1) Deficiency. The animal is unable to stand and is seized with severe clonic spasms particularly when handled. The muscles are contracted resulting in extension of the limbs and in a raised position of the head. After being photographed this animal received vitamin B (B_1) by intravenous injection (see Fig. 8). (Photograph reproduced through the courtesy of the *American Journal of Physiology.*)

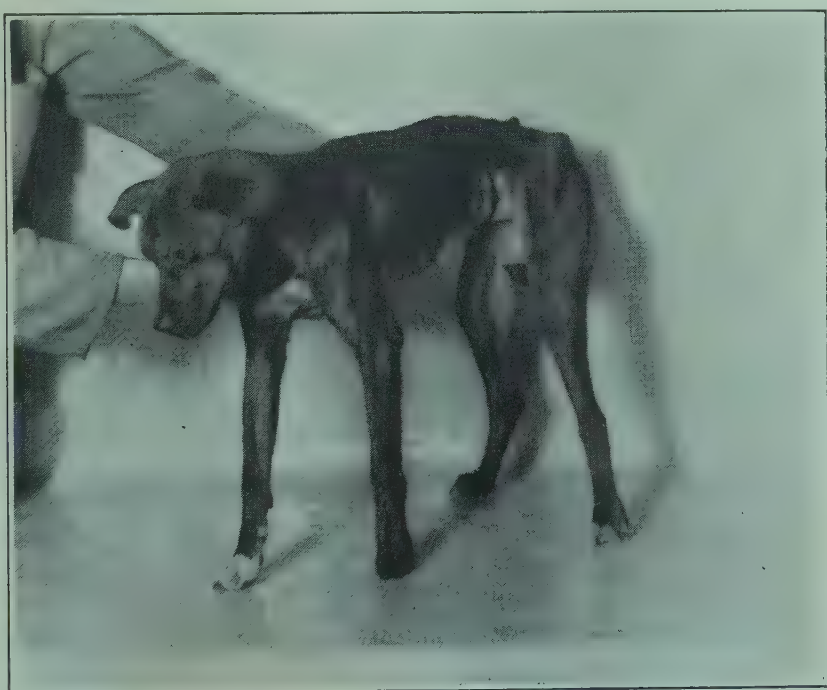

FIG. 8

Same Dog as Shown in Fig. 7, Photographed Four Hours and Ten Minutes After Receiving Vitamin B (B_1) by Injection into the Jugular Vein. The muscles are relaxed and the animal no longer exhibits clonic spasms when handled. The dog is also able to walk, the only manifestation of vitamin B (B_1) deficiency now apparent being a moderate spasticity of the muscles of the hind limbs resulting in a spastic gait. (Photograph reproduced through the courtesy of the *American Journal of Physiology.*)

Islands, prepares an extract of rice polishings called *tiki-tiki* which can be taken by mouth and which represents a reasonable concentration of vitamin B. This material is distributed among the natives as a prophylactic and curative public health measure as part of a program directed toward the eradication of beriberi. The public health laboratory at Batavia, Java, also prepares a concentrate suitable for general distribution. The notable work of Jansen and Donath (1927) resulting in the isolation of vitamin B in crystalline form was done at Batavia. As a result of the activities of the public health service in Java great strides have been taken toward the complete disappearance of beriberi from the Dutch East Indian possessions.

In Japan considerable use is made of the rice polish extract known as *oryzanin* and first prepared by Suzuki and associates (1912). The laboratory of biochemistry at Oxford University, England, through the activities of Peters and associates has likewise made valuable contributions toward the preparation of concentrates suited for clinical use.

As part of the research program reported in this monograph our own laboratory has devoted considerable attention to this problem. In this work we have used a pigeon technique as a means of rapid assay of various chemical fractions (Block, Cowgill and Klotz, 1932), and have made some chemical observations of interest (Block and Cowgill, 1932a, b, and 1934). A product has finally been obtained which is comparatively easy to prepare in concentrated sterile form suitable for injection intravenously, intramuscularly and subcutaneously (Stuart, Block and Cowgill, 1934). The fundamental discovery upon which the preparation of this product is based was made by Dr. Stuart. The availability of this material in large quantity should make it possible for clinicians to study the many problems outlined in the preceding pages and to determine the degrees of usefulness and limitations of vitamin B therapy. If these trials are made with concentrates of known vitamin B content, as expressed in international or other recognized units, it should be possible eventually to place vitamin B therapy on a definitely quantitative basis.

CHAPTER XVI

SUMMARY

IN THIS monograph are presented the results of a research designed to determine the human requirement for vitamin B. As indicated in the opening chapter, it is not feasible to study this problem directly in the human species because serious shortage of this dietary factor is associated with appearance of the disease beriberi. It has been necessary, therefore, to adopt an indirect approach to the problem. It was reasoned that if some common relationship should be found to hold for quantitative data derived from several animal species, there would be some justification for believing that this same relationship holds for the human species. Therefore measurements were made of the amounts of a given vitamin B concentrate required by different sized mice, rats, pigeons and dogs. The several groups of data thus obtained were studied and a mathematical relationship common to all of them was discovered. The formula thus derived suggests that the *body weight*, the *total metabolism* or *calories*, and the *maximum normal weight* of the species are the three important variables determining the vitamin B requirement. Experiments designed to test the implications of the formula were conducted on pigeons and dogs and confirmation obtained.

From these data a formula applicable to the *human* species was derived. This expression was tested by a study of the vitamin B content of numerous human dietaries (*a*) which were known to have been used by persons who developed beriberi, and (*b*) which were not associated with appearance of this disease. The amounts of vitamin estimated to be furnished by these various diets were compared with the requirements of the individuals who subsisted upon them in order to determine their adequacy as predicted by the formula. The results of such a study were also compared with the facts known concerning the incidence of beriberi in the respective groups studied. As the data reviewed in the preceding chapters indicate, there was excellent agreement of the predictions, based

on the formula, with the facts concerning the presence or absence of beriberi. Of the beriberi groups studied, only 8.6 percent failed to show good agreement.

Numerous clinical implications of this research present themselves for consideration. Some of them appear to explain many interesting facts relating to beriberi; others are significant in that they indicate possible applications of this research in the clinics of North America and other countries where manifest beriberi is rare, but where there may nevertheless be conditions in which shortage of vitamin B is an important factor. These are discussed in some detail.

It may be objected that in the present study of beriberi diets most of the rations examined were used many years ago. In reply let me state that all of the beriberi diets, which have been reported in the literature in sufficient detail to enable one to make a reasonably accurate estimation of vitamin B content, and which have been available to me, have been examined. Many epidemics of the disease are recorded but without sufficiently detailed statements as to the particular rations used. It was felt that publication now of the data contained in this monograph would be of greater service than to delay such a report in an endeavor to secure and to include in it recently obtained new data. The most important diets to study now are those of individuals and of small groups such as families exhibiting beriberi. Estimations of these cases should be much more significant in establishing the validity or falsity, and limitations of the results obtained thus far. In order to obtain these more critical data it will be necessary to secure the cooperation of numerous investigators in different parts of the world. Study of the material presented in this monograph should enable various interested students of beriberi to understand what data are required for further elucidation of this problem. As an example of the possibilities in this field consider the situation in Brazil where many clinicians do not believe that beriberi is a dietary deficiency. Even as late as December, 1932, we read in the *Journal of the American Medical Association* of an epidemic of beriberi in the island of Fernando de Noronha in the state of Pernambuco, Brazil:

> The government of the state sent a committee of physicians to study the causes and to control the epidemic. . . . The commissioners studied the climate and hy-

gienic conditions of housing, prisons, food and water supply, as well as the epidemiologic, bacteriologic and clinical aspects and pathogenesis of the disease. . . . The food for the garrison is more or less varied but the prisoners are fed only with beans, food prepared with flour and salted and dried beef. The cases of beriberi observed apparently were not caused by Bacillus coli-communis *nor were they due to alimentary deficiency*, since most of the cases observed were in persons who had the best kind of food. (Italics are mine.)

The reader will recall that one of the diets examined in relation to the occurrence of beriberi was that used in the Pudoh Gaol, Selangor, and described by Wright as a "correct and liberal diet on which convicts yet constantly incurred beriberi;" an estimate of the vitamin content of this ration, however, resulted in the finding that it was borderline with respect to its adequacy. It is not unlikely that quantitative examination of various Brazilian diets known to be associated with beriberi will reveal that these rations do not furnish a sufficient amount of vitamin B. Such a result, considered along with complications of fever, diarrhea, and related conditions, may offer a ready explanation of the presence of beriberi. By such a study it may be possible to settle the controversy concerning the etiology of beriberi in South America. It is with an expression of the hope that my colleagues throughout the world will be stimulated to secure these additional data that I close this monograph.

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APPENDIX

Vitamin b (B_1) Index Values of Foods

This table is based on Table 21 (see p. 87 *et seq.*) and gives the vitamin B (B_1) index values in terms of the *1934 International unit* as well as that of the author.

FOOD	VITAMIN INDEX VALUE PER GRAM	
	Milligram-Equivalent Unit (Author)	International Unit (1934)
Grains and Grain Products:		
Adlay	5.5	.28
Atta, crude	23	1.15
Barley:		
" husked	20	1.00
" kernel	20	1.00
" pearled	3	.15
Buckwheat	40	2.00
Cambu	16	.80
Cholam	15	.75
Corn:		
" whole kernel	20	1.00
" " "	20	1.00
" meal, old process, low grade	20	1.00
" " , " " , better grade	15	.75
" " , new process	5	.25
" sweet, canned comm'l	10	.50
Dari	20	1.00
Indian flour, pure unbleached	23	1.15
Macaroni	3	.15
Millet	26	1.30
Oatmeal	22	1.10
Rice:		
" brown	20	1.00
" "dead"	3	.15
" glutinous	5.5	.28
" polished	1.6	.80
" polishings	84	4.20
" whole, parboiled	15	.75
Rye	20	1.00
Wheat:		
" bran	40	2.00
" flour	3	.15
" germ	135	6.75
" middlings	75	3.75
" whole	20	1.00
" bread, white, water	2	.10
Pulses:		
Bean, coffee, roasted	0	0
" , frijoles (New Mexico)	20	1.00
" , haricot	20	1.00
" , red kidney	35	1.75
" , lima	20	1.00
" , navy, baked	10	.50
" , soy	23	1.15
" , in human diets, kind not stated	20	1.00
Cicer arientinum (yellow)	20	1.00
" " (red)	20	1.00
Dhal	23	1.15
Lentils:		
" (*Phaseolus mungo*)	26	1.30
" (" *radiatus*)	23	1.15
Peanut	40	2.00
Peas, whole dried green	26	1.30
" , raw, ungraded	15	.75
" , canned, in human diets	8	.40

APPENDIX—*Continued*

FOOD	VITAMIN INDEX VALUE PER GRAM: Milligram-Equivalent Unit (Author)	VITAMIN INDEX VALUE PER GRAM: International Unit (1934)
Nuts:		
Almonds, ground	20	1.00
" , whole	20	1.00
Chestnuts	20	1.00
Cocoanut, ripe	4	.20
" , water	0	0
Filbert, husked	40	2.00
Hazelnut	40	2.00
Nuts, in human diets, kind not stated	20	1.00
Pecan	20	1.00
Walnut, black	12	.60
Vegetables: Roots:		
Artichoke	10	.50
Aspaargus	14	.70
Beet	2.4	.12
Carrot, raw	3.7	.19
" , boiled	2.8	.14
Leeks	10	.50
Onions	2.7	.14
" , in Japanese diets	10	.50
Parsnips	14	.70
Poi (Hawaiian food, from taro)	6	.30
Potato, in human diets	3.8	.19
Radish	6.2	.31
" , pickled Japanese, "takuwan"	30	1.50
Rutabagas	2.4	.12
Sprouts, mung bean, raw	4	.20
" , " " , cooked	3.6	.18
Sweet potato	3.0	.15
Taro	7	.35
Turnip	2.4	.12
Vegetables: leaves, stalks and fruits:		
Cabbage, etiolated leaves	4.0	.20
" , Chinese, fresh	4.5	.23
" , " , salted	5.3	.27
" , " , bran-salted	25	1.25
Cauliflower	2.4	.12
Celery	2.4	.12
Collards, raw	11	.55
" , cooked	5.5	.28
Cucumbers, raw	3.4	.17
, pickles	1.7	.09
Eggplant	2.4	.12
Greens, raw turnip	11	.55
" , cooked turnip	11	.55
" , in human dietary, kind not stated	10	.50
Kale	4	.20
Kohlrabi	2.3	.12
Lettuce, greenhouse	4.2	.21
Limu (fresh water algae):		
" eleele	2	.10
" lipoa	1.3	.07
Peppers, green	2.2	.11
Pumpkin, raw	3.4	.17
" , canned	1.7	.09
Rhubarb	2.4	.12
Spinach, in human dietaries	2.4	.12
" , New Zealand; fresh	6.0	.30
Squash	3.4	.17
Stringbeans, raw, fresh	3.1	.16
" , in human dietaries	2.2	.11
Taro leaves	4	.20
Tomato, pulp	2.6	.13
" , juice, commercial	2.8	.14
" , dried	36	1.80
Watercress	5.5	.28

APPENDIX—*Continued*

FOOD	VITAMIN INDEX VALUE PER GRAM	
	Milligram-Equivalent Unit (Author)	International Unit (1934)
Fruits:		
Apple	2.2	.11
" , dried	6.7	.34
Apricot, fresh	2.2	.11
" , dried	6.7	.34
Avocado (pulp)	8.0	.40
Banana	2.9	.15
Berries, in human diets	2.2	.11
Cantaloupe, fresh	2.2	.11
Dates: "Hayany"	5.0	.25
" : "Deglet Noor"	2.5	.13
Grapes	3.0	.15
" , canned	1.5	.08
Hawaiian breadfruit, cooked	4	.20
Lemon, pulp	3.3	.17
Musk melon	2.2	.11
Orange, pulp	5.6	.28
" , juice	3.3	.17
Papaya, fresh	1.9	.10
Peaches, fresh	2.2	.11
" , canned	2.2	.11
Pears, Kiefer, raw	4.2	.21
Plantain, raw	2.7	.14
Prunes, raw	3.8	.19
" , dried	14	.70
Raisins	7.0	.35
Strawberry	2.2	.11
Yautia, raw fruit	7.4	.37
Animal Tissues:		
Beef: heart	15	.75
" : brain, cerebellum	10	.50
" : liver	32	1.60
" : muscle	5	.25
" : " , "dried beef"	10	.50
Chicken, liver	10	.50
" , muscle	5	.25
Pork: heart	7.5	.38
" : liver	10	.50
" : fresh lean muscle	37	1.85
" ; smoked ham	37	1.85
" , lean loin chops	37	1.85
" : Bologna sausage	36	1.80
" : pork sausage	24	1.20
" : head	24	1.20
" : ham, medium, fat	24	1.20
" : ham, fat	22	1.10
" : bacon, smoked, med. fat	18	.90
" : salt pork	14	.70
" : sides	16	.80
" : jowl	11	.55
" : shoulder	24	1.20
" : fat; lard	11	.55
Sheep: brain	7.0	.35
" : muscle, "mutton"	5	.25
Veal	5	.25
Sea-Foods:		
Clams, fresh	1	.05
Fish, fresh, in human diets	4.5	.23
" , dried " "	8	.40
Herring, smoked	8	.40
Oysters, fresh	7.5	.38
" , cooked	6.0	.30

APPENDIX—*Concluded*

FOOD	VITAMIN INDEX VALUE PER GRAM	
	Milligram-Equivalent Unit (Author)	International Unit (1934)
Eggs:		
Hen's egg: solids, commercial	20	1.00
" " : whole, edible	5.6	.28
" " : yolk, raw	9.5	.48
Milk and Milk Products:		
Butter (from cow's milk)	8	.40
Buttermilk (from cow's milk)	2.2	.11
Cheese, kind not stated	2	.10
Cow's Milk: malted	33	1.65
" " : skimmed, dried	13	.65
" " : " , powder, spray process	22	1.10
" " : " , fresh	2.2	.11
" " : " , dried	20	1.00
" " : " , fresh	3.6	.18
Cream, as purchased	4.2	.21
Human Milk: American women	2.4	.12
Miscellaneous:		
Honey	0	0
" , comb	0	0
Molasses: cane	150	7.50
" , beet	29	1.45
" , sorghum	19	.95
Sugar cane juice	0	0
Special Vitamin B Preparations:		
From liver	110	5.5
From rice polishings:		
"Tiki-tiki"	75	3.75
International standard adsorbate	2,000	100.00
"Adsorbed Vitamin B (Lilly) 889071-C"	4,500	225.00
Vitamin B_1 Extract, Sterile Solution (P-27034) (for parenteral admin.)	1,000	50.00
From wheat germ:		
"Bemax"	130	6.50
Yeast and Yeast Preparations:*		
Yeast, "Marmite"	130	6.50
Yeast Vitamin Powder (Harris) lot 985	1,000	50.00

* From the data shown in Table 21 it is evident that yeasts may vary widely in content of vitamin B (B_1). Yeasts with values of 180–200 mg.eq. per gram, or 9–10 International Units per gram would rate as excellent in vitamin content.

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